Interventions for treating proximal humeral fractures in adults (Review)

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[Intervention Review]

Interventions for treating proximal humeral fractures in adults

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ABSTRACT

Background

Fracture of the proximal humerus, often termed shoulder fracture, is a common injury in older people. The management of these fractures varies widely. This is an update of a Cochrane Review first published in 2001 and last updated in 2012.

Objectives

To assess the effects (benefits and harms) of treatment and rehabilitation interventions for proximal humeral fractures in adults.

Search methods

We searched the Cochrane Bone, Joint and Muscle Trauma Group Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, and other databases, conference proceedings and bibliographies of trial reports. The full search ended in November 2014.

Selection criteria

We considered all randomised controlled trials (RCTs) and quasi-randomised controlled trials pertinent to the management of proximal humeral fractures in adults.

Data collection and analysis

Both review authors performed independent study selection, risk of bias assessment and data extraction. Only limited meta-analysis was performed.

Main results

We included 31 heterogeneous RCTs (1941 participants). Most of the 18 separate treatment comparisons were tested by small single-centre trials. The main exception was the surgical versus non-surgical treatment comparison tested by eight trials. Except for a large multicentre trial, bias in these trials could not be ruled out. The quality of the evidence was either low or very low for all comparisons except the largest comparison.

Nine trials evaluated non-surgical treatment in mainly minimally displaced fractures. Four trials compared early (usually one week) versus delayed (three or four weeks) mobilisation after fracture but only limited pooling was possible and most of the data were from

one trial (86 participants). This found some evidence that early mobilisation resulted in better recovery and less pain in people with mainly minimally displaced fractures. There was evidence of little difference between the two groups in shoulder complications (2/127 early mobilisation versus 3/132 delayed mobilisation; 4 trials) and fracture displacement and non-union (2/52 versus 1/54; 2 trials).

One quasi-randomised trial (28 participants) found the Gilchrist-type sling was generally more comfortable than the Desault-type sling (body bandage). One trial (48 participants) testing pulsed electromagnetic high-frequency energy provided no evidence. Two trials (62 participants) provided evidence indicating little difference in outcome between instruction for home exercises versus supervised physiotherapy. One trial (48 participants) reported, without presentable data, that home exercise alone gave better early and comparable long-term results than supervised exercise in a swimming pool plus home exercise.

Eight trials, involving 567 older participants, evaluated surgical intervention for displaced fractures. There was high quality evidence of no clinically important difference in patient-reported shoulder and upper-limb function at one- or two-year follow-up between surgical (primarily locking plate fixation or hemiarthroplasty) and non-surgical treatment (sling immobilisation) for the majority of displaced proximal humeral fractures; and moderate quality evidence of no clinically important difference between the two groups in quality of life at two years (and at interim follow-ups at six and 12 months). There was moderate quality evidence of little difference between groups in mortality in the surgery group (17/248 versus 12/248; risk ratio (RR) 1.40 favouring non-surgical treatment, 95% confidence interval (CI) 0.69 to 2.83; P = 0.35; 6 trials); only one death was explicitly linked with the treatment. There was moderate quality evidence of a higher risk of additional surgery in the surgery group (34/262 versus 16/261; RR 2.06, 95% CI 1.18 to 3.60; P = 0.01; 7 trials). Although there was moderate evidence of a higher risk of adverse events after surgery, the 95% confidence intervals for adverse events also included the potential for a greater risk of adverse events after non-surgical treatment.

Different methods of surgical management were tested in 12 trials. One trial (57 participants) comparing two types of locking plate versus a locking nail for treating two-part surgical neck fractures found some evidence of slightly better function after plate fixation but also of a higher rate of surgically-related complications. One trial (61 participants) comparing a locking plate versus minimally invasive fixation with distally inserted intramedullary K-wires found little difference between the two implants at two years. Compared with hemiarthroplasty, one trial (32 participants) found similar results with locking plate fixation in function and re-operation rates, whereas another trial (30 participants) reported all five re-operations occurred in the tension-band fixation group. One trial (62 participants) found better patient-rated (Quick DASH) and composite shoulder function scores at a minimum of two years follow-up and a lower incidence of re-operation and complications after reverse shoulder arthroplasty (RSA) compared with hemiarthroplasty.

No important between-group differences were found in one trial (120 participants) comparing the deltoid-split approach versus deltopectoral approach for non-contact bridging plate fixation, and two trials (180 participants) comparing 'polyaxial' and 'monaxial' screws in locking plate fixation. One trial (68 participants) produced some preliminary evidence that tended to support the use of medial support locking screws in locking plate fixation. One trial (54 participants) found fewer adverse events, including re-operations, for the newer of two types of intramedullary nail. One trial (35 participants) found better functional results for one of two types of hemiarthroplasty. One trial (45 participants) found no important effects of tenodesis of the long head of the biceps for people undergoing hemiarthroplasty.

Very limited evidence suggested similar outcomes from early versus later mobilisation after either surgical fixation (one trial: 64 participants) or hemiarthroplasty (one trial: 49 participants).

Authors' conclusions

There is high or moderate quality evidence that, compared with non-surgical treatment, surgery does not result in a better outcome at one and two years after injury for people with displaced proximal humeral fractures involving the humeral neck and is likely to result in a greater need for subsequent surgery. The evidence does not cover the treatment of two-part tuberosity fractures, fractures in young people, high energy trauma, nor the less common fractures such as fracture dislocations and head splitting fractures.

There is insufficient evidence from RCTs to inform the choices between different non-surgical, surgical, or rehabilitation interventions for these fractures.

PLAIN LANGUAGE SUMMARY

Interventions for treating shoulder fractures in adults

Background

Fracture of the top end of the upper arm bone (proximal humerus) is a common injury in older people. It is often called a shoulder fracture. The bone typically fractures (breaks) just below the shoulder, usually after a fall. Most of these fractures occur without breaking the skin lying over the fracture. The injured arm is often supported in a sling until the fracture heals sufficiently to allow shoulder movement. More severe (displaced) fractures may be treated surgically. This may involve fixing the fracture fragments together by various means. Alternatively, the top of the fractured bone may be replaced (half 'shoulder' replacement: hemiarthroplasty). More rarely, the whole joint, thus including the joint socket, is replaced (total 'shoulder' replacement). Physiotherapy is often used to help restore function.

Results of the search

We searched medical databases up to November 2014 and included 31 randomised studies with a total of 1941 participants. Most of the 18 treatment comparisons were tested by one study only. The best evidence was from eight studies, one of which was a relatively large multicentre study; these investigated whether surgery gave a better result than non-surgical treatment for displaced fractures.

Key results

Nine trials evaluated non-surgical treatment in usually less severe fractures. One trial found a type of arm sling was generally more comfortable than a type of body bandage. There was some evidence that early mobilisation (within one week), compared with delayed mobilisation (after three weeks), resulted in less pain and faster recovery in people with 'stable' fractures. Two studies provided weak evidence that many patients could generally achieve a satisfactory outcome when given sufficient instruction to pursue exercises on their own.

Eight studies, involving 567 participants with displaced fractures, compared surgical versus non-surgical treatment. Pooled results from the five most recent trials showed that there were no important differences between the two approaches for patient-reported measures of function and quality of life at 6, 12 and 24 months. There was little difference between the two groups in mortality. Twice as many surgical group patients had additional or secondary surgery. More surgical group patients had adverse events.

Twelve trials (744 participants) tested different methods of surgical treatment. There was weak evidence of some differences (e.g. in complications) between some interventions (e.g. different devices or different ways of using devices).

There was very limited evidence suggesting similar outcomes for early versus delayed mobilisation after either surgical fixation or hemiarthroplasty.

Quality of the evidence

Most of the 31 studies had weaknesses that could affect the reliability of their results. We considered that the evidence was either of high or moderate quality for the results of the surgical versus non-surgical treatment comparison, which means that we are pretty certain these results are reliable. We considered that the evidence for other comparisons was of low or very low quality, which means we are unsure of these results.

Conclusions

Surgery does not result in a better outcome for the majority of people with displaced proximal humeral fractures and is likely to result in a greater need for subsequent surgery. Otherwise, there is not enough evidence to determine the best non-surgical or, when selected, surgical treatment for these fractures.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Surgical versus non-surgical treatment for proximal humeral fractures

Patient or population: [mainly older] adults with most types of displaced proximal humeral fractures[1] (8 trials)
Settings: hospital (tertiary care)
Intervention: surgery, various: mainly open reduction and internal fixation (ORIF) with locking plate or hemiarthroplasty
Comparison: non-surgical treatment, mainly sling 'immobilisation'; more rarely, closed reduction/manipulation of the fracture (2 trials)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Non-surgical treatment	Surgical treatment				
Functional scores[2] (higher = better outcome) Follow-up: 1 year		The mean difference in function (overall) in the surgery groups was **0.07 standard deviations higher** (0.12 lower to 0.26 higher)	**SMD 0.07** (-0.12 to 0.26)	419 participants (5 studies)	⊕⊕⊕⊕ **high**[3]	This does not represent a clinically important difference: • 0.2 represents a small difference, 0.5 a moderate difference and 0.8 a large difference. Thus, based on this 'rule of thumb', there is little difference between the two groups. At most, the extreme range of the 95% CI includes a minimal difference in favour of surgery at one year. • All of the best estimates of between-group differences for the individual outcome scores[2] were much smaller than their associated MCIDs

Functional scores[4] (higher = better outcome) Follow-up: 2 years		The mean difference in function (overall) in the surgery groups was **0.07 standard deviations higher** (0.14 lower to 0.28 higher)	(SMD 0.07, 95% CI -0.14 to 0.28)	351 participants (4 studies)	⊕⊕⊕⊕ **high**[5]	This does not represent a clinically-important difference. • 0.2 represents a small difference, 0.5 a moderate difference and 0.8 a large difference. Thus, based on this 'rule of thumb', there is little difference between the two groups. At most, the extreme range of the 95% CI includes a minimal difference in favour of surgery at two years. • All of the best estimates of between-group differences for the individual outcome scores[4] were much smaller than their associated MCIDs
Quality of life assessment: EuroQol (0: dead to 1: best health) Follow-up: 2 years	The mean EuroQol score ranged across control groups from 0.7 to 0.85	The mean EuroQol score in the surgery groups was 0.03 higher, (0.01 lower to 0.08 higher)		354 participants (4 studies)	⊕⊕⊕◯ **moderate**[6]	The MCID of 0.12 was outside the 95% CI at this time period and at 6 months (MD 0.04, 95% CI 0.01 to 0.08) and 12 months (MD 0.02, 95% CI -0.02 to 0.06)
Quality of life: SF-12 Physical Component Score (0 to 100: best) Follow-up: 2 years	The mean SF-12 PCS was **44.1**	The mean SF-12 PCS in the surgery group was **1.10 higher** (1.99 lower to 4.19 higher)		210 participants (1 study)	⊕⊕⊕◯ **moderate**[7]	A similar lack of clinically important difference[8] was noted at 6 and 12 months. This measure may not be sensitive to recovery from this injury

Mortality Follow-up: up to 2 years	**52 per 1000**[8]	**73 per 1000** (4 to 147)	**RR 1.40** (0.69 to 2.83)	596 participants (6 studies)	⊕⊕⊕◯ **moderate**[9]	Surgery resulted in 21/1000 more deaths up to 2 years (95% CI 48 fewer to 95 more) Where reported, none of the deaths was related to their fracture or treatment with the exception of one early death due to venous thromboembolism in the surgical group of one trial
Additional surgery (re-operation or secondary surgery) Follow-up: up to 2 years	**40 per 1000**[9]	**83 per 1000** (47 to 144)	**RR 2.06** (1.18 to 3.60)	523 participants (7 studies)	⊕⊕⊕◯ **moderate**[10]	Surgery resulted in 43/1000 more patients having additional surgery up to 2 years (95% CI 7 to 104 more) One trial (250 participants) also reported on additional shoulder-related therapy (7/1254 versus 4/125; RR 1.75 favouring non-surgical therapy, 95% CI 0.53 to 5.83)
Adverse events / complications - Number of patients with complications Follow-up: 2 years	**184 per 1000**[9]	**239 per 1000** (147 to 389)	**RR 1.30** (0.80 to 2.11)	250 participants (1 study)	⊕⊕⊕◯ **moderate**[11]	Surgery resulted in 55/1000 more patients having adverse events up to 2 years (95% CI 37 fewer to 205 more) All 8 trials reported on individual complications, the pattern of distribution generally reflecting the expected: e.g. infection 8/

				279 cases after surgery versus 0/280 cases after non-surgical treatment

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; MCID: minimal clinically important differences; **RR:** risk ratio; **SMD:** standardised mean difference

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

1. The inclusion/exclusion criteria varied among the trials: one (30 participants) included 2-, 3- or 4-part fractures; one (60 participants) included only 3-part fractures that included surgical neck; two (90 participants) included 3- or 4-part fractures, three (137 participants) included only 4-part fractures. The final trial (250 participants) included ' ' displaced fracture of the proximal humerus that involved the surgical neck", resulting in a few 1-part (but confirmed as still ' ' displaced") as well as 2-, 3- and 4-part fractures. The majority of the fractures (146/250 = 58.4%) in the largest trial were either 2-part (128) or 1-part (18) fractures. Several trials included further criteria; for example, the largest trial explicitly excluded fracture dislocations (i.e. fractures with an associated dislocation of the injured shoulder joint). Consideration is also needed of other inclusion and exclusion criteria, including multiple trauma, clear indications for surgery (severe soft-tissue compromise), and co-morbidities precluding surgery or anaesthesia
2. Patient-reported functional scores were the Disability of the Arm, Shoulder, and Hand questionnaire (DASH; 2 trials), the Oxford Shoulder Score (OSS; 1 trial); the American Shoulder and Elbow Surgeons (ASES; 1 trial) and Simple Shoulder Test (SST; 1 trial)
3. Although the evidence was first downgraded by one level for study limitations, reflecting a high risk of performance bias relating to lack of blinding in four single-centre trials, the consistency in the results of these and the fifth and largest trial, where the analysis indicated that the study design limited the risk of bias relating to the inevitable lack of blinding, resulted in an upgrade
4. Patient-reported functional scores were the Disability of the Arm, Shoulder, and Hand questionnaire (DASH; 2 trials), the Oxford Shoulder Score (OSS; 1 trial); and the American Shoulder and Elbow Surgeons (ASES; 1 trial)
5. The evidence was downgraded by one level for study limitations, reflecting a high risk of performance bias relating to lack of blinding in 3 single-centre trials. There was, however, consistency in the results of these and the fourth and largest trial, where the analysis indicated that the study design limited the risk of bias relating to the inevitable lack of blinding, resulting in an upgrade
6. The evidence was downgraded by one level for inconsistency, reflecting the statistical heterogeneity ($Chi^2 = 6.76$, df = 3 (P = 0.08); $I^2 = 56\%$), but also data from two trials (102 participants) from the same centre that found minimal clinically important differences favouring surgery
7. The evidence was downgraded one level for imprecision, reflecting that these data were from one trial alone
8. A minimal clinically important difference for the SF-12 PCS was assumed to be 6.5. Notably, a similar finding applied for the between-group differences in SF-12 Mental Component Scores, but the direction of effect favoured non-surgical treatment

9. Assumed risk is the median control group risk across studies
10. The evidence was downgraded one level for imprecision.
11. The evidence was downgraded one level for inconsistency (heterogeneity: $Chi^2 = 8.50$, df = 6 (P = 0.20); $I^2 = 29\%$), which was greater for the two years follow-up data (heterogeneity: $Chi^2 = 7.29$, df = 3 (P = 0.06); $I^2 = 59\%$). At two years, three trials (160 participants) reported more additional surgery in the surgery group, but the trial (250 participants) contributing 65% of the weight of the evidence recorded equal numbers of participants (11 versus 11) undergoing additional surgery.

BACKGROUND

Description of the condition

Proximal humeral fractures account for approximately six per cent of all adult fractures (Court-Brown 2006). Their incidence rapidly increases with age, and women are affected between two and three times as often as men (Court-Brown 2006; Lind 1989). Many patients who sustain a proximal humeral fracture are old and their bones are osteoporotic. Court-Brown 2001 found that 87% of these fractures in adults resulted from falls from standing height. Palvanen 2006 found that the incidence of osteoporotic-related fractures of the proximal humerus in Finland had tripled between 1970 and 2002 to 105 per 100,000 people aged 60 or above. An epidemiological study of upper-limb fractures occurring in 2009 in the USA reported an incidence of 60 proximal humeral fractures per 100,000 people overall, with four-fold increased incidence of 253 per 100,000 in those aged 65 or older (Karl 2015).

Most proximal humeral fractures are closed fractures in that the overlying skin remains intact. The most commonly used classification of shoulder fractures is that of Neer (Neer 1970). Neer considered four anatomical segments of the proximal humerus - the articular part, the greater tuberosity, the lesser tuberosity and the humeral shaft. These may be affected by fracture lines but are only considered as a 'part' if displaced by more than one centimetre or 45 degrees angulation from each other. Fractures, regardless of the number of fracture lines present, which did not meet the criteria for displacement of any one segment with respect to the others were considered 'minimally displaced'; these are sometimes referred to as one-part fractures. Neer's other categories, two-part, three-part and four-part fractures all involved the displacement or angulation of some or all of the above four segments. Each of these fracture types may be potentially associated with an anterior or posterior humeral head dislocation.

At initial presentation, it may be difficult to delineate the exact pathoanatomical pattern of the fracture even with sophisticated imaging. In any event, this may not correlate with the extent to which the vascularity (blood supply) of the humeral head is compromised. The vascularity of the proximal humerus is a primary focus of another widely used classification system for these fractures, the AO classification system (Muller 1991), which was updated in conjunction with the OTA classification in 2007 (Marsh 2007). There are three main types (A, B, C), which in turn are further divided into three groups, each with a further three subgroups. Type A fractures are "extra-articular, unifocal, with intact vascular supply"; type B fractures are "extra-articular, bifocal, with possible vascular compromise"; and type C fractures are "articular, with a high likelihood of vascular compromise" (Robinson 2008).

Many proximal humeral fractures are only minimally displaced. Neer's estimate (Neer 1970) that approximately 85% of all proximal humeral fractures are minimally displaced, in that no bone fragment is displaced by more than one centimetre, or angulated by more than 45 degrees is often cited (Koval 1997). However, a lower figure of 49% was reported in a prospective consecutive series of over 1000 proximal humeral fractures (Court-Brown 2001).

Description of the intervention

Non-surgical (conservative) treatment is generally the accepted treatment option for minimally displaced fractures, and often used also for people with displaced fractures. Non-surgical treatment usually involves a period of immobilisation, such as in an arm sling, followed by physiotherapy and exercises. Non-surgical treatment can include closed reduction, where the displaced bone fragments are reduced using various manoeuvres while the arm is under traction. Various aspects of non-surgical treatment, such as the arm sling and collar and cuff, are illustrated online (AO 2015). Older types of bandages, such as the Desault and Velpeau, are illustrated in Brorson 2011a.

Surgery is usually reserved for displaced and unstable fractures and those with more complicated fracture patterns. Surgical interventions include:

- closed reduction and percutaneous stabilisation using pins or wires;
- external fixation;
- open reduction and plating, for example buttress plates, angle blade plates and proximal humeral locking plates;
- open reduction and fixation using a tension-band principle;
- intramedullary nailing, either antegrade or retrograde insertion (intramedullary nails usually offer the option of locking screws, which are inserted into fracture fragments then transverse the nail, providing additional fracture stability);
- hemiarthroplasty (replacement of the humeral head);
- total shoulder replacement (replacement of the entire joint; both the 'ball' (humeral head) and 'socket' (glenoid)). There are two distinct types: anatomical and reverse shoulder arthroplasty. In reverse arthroplasty the joint polarity is reversed such that the ball is on glenoid side and the socket (fixed on a stem) on the humeral side.

Post-operative treatment generally involves a period of immobilisation followed by physiotherapy and exercises.

How the intervention might work

Immobilisation of the injured limb provides support and pain relief during healing. However, there is a risk of the shoulder becoming stiff and painful with substantial reduction of function. Subsequent physiotherapy and exercises aim to restore function and mobility of the injured (or operated) arm. Malunion of proximal humeral fractures may result in impingement or compromised function of the 'rotator cuff' of muscles and tendons that surrounds the shoulder joint. Persistent pain and painful pseudoparalysis are common indications for late surgery.

After reduction or repositioning of the fractured parts, surgical fixation using various techniques aims to stabilise the reduced fracture and restore joint integrity. Surgical stabilisation of the fracture may also allow earlier movement of the shoulder and elbow, preventing stiffness. Surgeons have often followed Neer's premise (Neer 1975) that head avascular necrosis is virtually guaranteed in a four-part fracture and have usually offered these patients a hemiarthroplasty, where the humeral head is replaced by an artificial part. An exception is often made for a specific type of four-part fracture, the valgus impacted four-part fracture, which was not mentioned initially in Neer's classification. This fracture, where the fractured parts are compressed towards each other, is less likely to lead to avascular necrosis of the humeral head, provided the lateral displacement of the head fragment is not excessive (Jakob 1991; Resch 1997). Bone quality also influences the appropriateness of any intervention and hence the long term clinical outcome. Furthermore, the patient's frailty may lead to a low rehabilitation drive and delay any recovery from both the initial trauma and any subsequent management.

Why it is important to do this review

Proximal humeral fractures are increasing in incidence, particularly in older people, and the short and long term consequences for individuals with these injuries and society are substantial (Palvanen 2006). There is considerable variation in practice, both in terms of definitive treatment such as surgical treatment for displaced fractures (Guy 2010) and rehabilitation (Hodgson 2006). Variation in practice includes that of the uptake of new implants, typically before their effectiveness has been evaluated, as illustrated for reverse shoulder arthoplasty in the USA (Schairer 2015). The costs of treating these fractures are also substantial and growing. The direct health-care costs, adjusted to 2007 prices, in the Netherlands of upper arm fractures, the majority of which were proximal humeral fractures, were EUR 4,440 per case with an overall annual cost of approximately EUR 40M (Polinder 2013). Polinder 2013 suggested that the increase in the cost of fracture care in 'elderly women' from a previous report of costs in the Netherlands was partly because of a higher incidence of surgery. This trend to increased surgery also applies in other countries such as the USA (Bell 2011). A very recently published report by the same team in the Netherlands estimated the medical costs per case in 2012, including hospitalisation, rehabilitation and nursing care, and, primarily in patients aged over 80 years, home care costs, were EUR 11,224 (Mahabier 2015). The estimated costs for lost productivity including time off work and other costs for those in work was EUR 20,374 per case in 2012. Schairer 2015 found the estimated mean hospital costs in 2011 in the USA were significantly higher for reverse shoulder arthroplasty than for hemiarthroplasty (USD 21,723 versus USD 18,122), a difference which was almost three times greater when it came to mean hospital charges (USD 75,849 versus USD 65,477). The often poor treatment outcome and the increasing incidence of these fractures, the increasing use of surgery and of reverse shoulder arthoplasty (Han 2015), high treatment costs and variations in practice all endorse the need for this review update.

The last two versions of this review noted the insufficiency of the evidence to inform practice, but also located ongoing trials that could potentially help to address this deficiency (Handoll 2007; Handoll 2010). This update continues the systematic review of the evidence for managing these fractures.

OBJECTIVES

To assess the effects (benefits and harms) of treatment and rehabilitation interventions for proximal humeral fractures in adults.

We defined a priori the following broad objectives:

- to compare different methods of non-surgical treatment (including rehabilitation);
- to compare surgical versus non-surgical treatment;
- to compare different methods of surgical treatment;
- to compare different methods of rehabilitation after surgical treatment.

We planned to study the outcomes in different age groups (initially, under versus over 65 years) and for different types of proximal humeral fractures.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised or quasi-randomised (method of allocating participants to a treatment that is not strictly random; e.g. by hospital record number) trials which compared two or more interventions in the management of fractures of the proximal humerus in adults.

Types of participants

We included adults with a fracture of the proximal humerus. Stratification was planned by fracture type (e.g. based on the Neer classification (Neer 1970) or the AO classification (Muller 1991)) and by age (under versus over 65 years) if possible. Trials including children were included provided either separate data for skeletally

mature participants were available or the proportion of children was small and, preferably, balanced in intervention groups.

Types of interventions

Non-surgical and surgical interventions, as exemplified in Description of the intervention, used in the treatment and rehabilitation of fractures of the proximal humerus. Pharmacological trials were excluded.

Types of outcome measures

The primary focus is on long term functional outcome, preferably measured at one year or more.

Primary outcomes

- Functional outcomes: patient-reported measures of upper-limb function (e.g. the Disability of the Arm, Shoulder, and Hand questionnaire (DASH), the Oxford Shoulder Score (OSS; Dawson 1996; Dawson 2009), and other validated shoulder rating scales).
- Activities of daily living and health-related quality-of-life scores (e.g. EuroQol (EQ-5D); Short-Form 36 (SF-36) and Short-Form 12 (SF-12; Ware 1996).
- Serious adverse events (e.g. death, deep infection, avascular necrosis, complex regional pain syndrome type 1) and need for substantive treatment, such as an operation.

Secondary outcomes

- Composite scores of subjectively and objectively rated function and overall outcome (e.g. Constant and Murley's score (Constant 1987); Neer's rating (Neer 1970)).
- Pain.
- Upper limb strength and range of movement.
- Less serious complications/adverse events of limited duration and impact (e.g. superficial infection, transient paraesthesia, skin irritation).
- Patient satisfaction with treatment, including cosmetic outcomes.
- Anatomical outcomes (e.g. radiological deformity).

Economic outcomes: each trial report was reviewed for cost and resource data, such as length of hospital stay and number of outpatient attendances, that would enable economic evaluation.

We based our judgement of clinically important between-group mean differences in measures of pain and function using the following minimal clinically important differences (MCID); alternative sources are listed after the main selected item in bold.

- ASES (0 to 100: best outcome) (rotator cuff disease): **12.01** (function-based) (Tashjian 2010).
- Constant score (0 to 100: best outcome) (proximal humerus fracture): **11.6** (anchor-based), 5.1 (distribution-based) (Van de Water 2014); (upper limb proximal diagnosis): MCID 10.2 (Schmitt 2004)
- DASH (0 to 100: worst outcome) (proximal humerus fracture): **13.0** (anchor-based), 8.1 (distribution-based) (Van de Water 2014); 15 recommended in DASH/QuickDASH
- EQ-5D (0 to 1: best outcome) (proximal humerus fracture): **0.12** (assessed in relation to a DASH MCID of 10) (Olerud 2011c)
- OSS (0 to 48: best outcome) (proximal humerus fracture): **11.4** (anchor-based), 5.1 (distribution-based) (Van de Water 2014)
- QuickDASH (0 to 100: worst outcome): **16** in DASH/QuickDASH; 8 (shoulder pain) (Mintken 2009)
- SF-12-PCS (0 to 100: best outcome) (physical component score) (upper limb proximal diagnosis): MCID **6.5** (Schmitt 2004)
- SST (0 to 12: best outcome) (rotator cuff disease): **2.05** (Tashjian 2010)
- UCLA (2 to 35: best outcome) (proximal humerus fracture): **2.4** (anchor-based), 2.0 (distribution-based) (Van de Water 2014)

Search methods for identification of studies

Electronic searches

We searched the Cochrane Bone, Joint and Muscle Trauma Group Specialised Register (10 November 2014), the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2014, Issue 10), MEDLINE (1966 to October Week 5 2014), MEDLINE In-Process & Other Non-Indexed Citations (7 November 2014), EMBASE (1988 to 2014 Week 45), CINAHL (Cumulative Index to Nursing and Allied Health Literature) (10 November 2014), AMED (Allied and Complementary Medicine) (1985 to 10 November 2014), and PEDro - Physiotherapy Evidence Database (10 November 2014).

In MEDLINE, we combined subject-specific terms with the sensitivity-maximizing version of the Cochrane Highly Sensitive Search Strategy for identifying randomised trials (Lefebvre 2011) (Appendix 1). Search strategies for CENTRAL, EMBASE, CINAHL, AMED and PEDro can also be found in Appendix 1. For this update, the search results were limited from January 2012 onwards. Details of the search strategies used for previous versions of the review are given in Handoll 2007, Handoll 2010 and Handoll 2012. We applied no language or publication restrictions.

We searched the WHO International Clinical Trials Registry Platform Search Portal, the ISRCTN registry, and ClinicalTrials.gov to identify ongoing and recently completed trials (10 November 2014) (see Appendix 1).

Searching other resources

We searched the reference lists of articles. We also included the findings from handsearches of the British Volume of the Journal of Bone and Joint Surgery supplements (1996 to 2006) and electronic searches of the The Bone and Joint Journal Orthopaedic Proceedings (10 November 2014) (see Appendix 1). We searched abstracts of the British Elbow and Shoulder Society annual meetings (2001 to 2013), the American Orthopaedic Trauma Association annual meetings (1996 to 2014), American Academy of Orthopaedic Surgeons annual meetings (2005, 2006, 2014), and the British Trauma Society annual scientific meetings (2012 and 2014). Prior to this update, we handsearched various orthopaedic proceedings and screened weekly downloads from AMEDEO (to 2007), the details of which can be found in Handoll 2012.

Data collection and analysis

Selection of studies

For this update, both review authors independently screened search results and assessed potentially eligible studies for inclusion. The initial decisions of trial eligibility were based on citations and, where available, abstracts and indexing terms. We obtained full articles and, where necessary to ascertain trial methods and status, one author (HH) sent requests for information to trial investigators. Study inclusion was by consensus. Titles of journals, names of authors or supporting institutions were not masked at any stage. Both authors performed independent study selection on the trials for which the other author was an investigator.

Data extraction and management

Both review authors independently completed a data extraction tool, which had been used in the previous version of the review, for each newly included trial. We recorded details of the study methods, participants, interventions and outcome assessment and results. Any differences that were clearly not transcription errors were discussed between review authors. Data management and entry into Review Manager (RevMan 2014) was mainly by one author (HH) with checks made by both review authors. When necessary, additional details of trial methodology or data, or both were requested from trialists.

Assessment of risk of bias in included studies

Both review authors independently assessed risk of bias for newly included trials, without masking of the source and authorship of the trial reports. HH checked between-rater and between-versions consistency in assessment at data entry. All inter-rater differences were resolved by discussion. We used the tool outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008a). This tool incorporates assessment of randomisation (sequence generation and allocation concealment), blinding (of participants, treatment providers and outcome assessment), completeness of outcome data, selection of outcomes reported and other sources of bias. We considered subjective and functional outcomes (e.g. functional outcomes, pain, clinical outcomes, complications) and 'hard' outcomes (death, reoperation) separately in our assessment of blinding and completeness of outcome data. We assessed two additional sources of bias: bias resulting from major imbalances in key baseline characteristics (e.g. age, gender, type of fracture); and performance bias such as resulting from lack of comparability in the experience of care providers.

Additionally, we assessed four other aspects of trial quality and reporting that would help us judge the applicability of the trial findings. The four aspects were: definition of the study population; description of the interventions; definition of primary outcome measures; and length of follow-up.

Measures of treatment effect

For each trial, risk ratios (RR) and 95% confidence intervals (CIs) were calculated for dichotomous outcomes, and mean differences (MD) and 95% CIs were calculated for continuous outcomes. Standardised mean differences (SMD) rather than mean differences were used when pooling data from continuous outcome measures based on different scoring schemes.

Unit of analysis issues

We remained aware of potential unit of analysis issues arising from inclusion of participants with bilateral fractures, and presentation of outcomes, such as total complications, by the number of outcomes rather than participants with these outcomes. There was just one patient with bilateral fractures (Kristiansen 1988) but there was insufficient information to quantify the small difference this would have made to study findings. We avoided the second described unit of analysis problem, mainly by reporting on incidences of individual complications.

Dealing with missing data

We contacted trialists for missing information, including for denominators and standard deviations. We performed intention-to-treat analyses where possible. Where there were missing standard deviations, we calculated these from other data (standard errors, 95% CIs, exact P values) where available. We did not impute missing standard deviations.

Assessment of heterogeneity

We assessed heterogeneity for pooled data from comparable trials by visual inspection of the analyses along with consideration of the chi² test for heterogeneity and the I² statistic (Higgins 2003). The

main quantitative assessment of heterogeneity was based on the I^2 statistic where the following interpretation from the *Cochrane Handbook for Systematic Reviews of Interventions* was used: 0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity; and 75% to 100% considerable heterogeneity (Deeks 2011).

Assessment of reporting biases

There are insufficient data thus far (a minimum of 10 trials is required) to merit the production of funnel plots to explore publication bias. The search for trials via conference proceedings and trial registration, together with the contacting of authors for information of trial status and progress has provided some insights on unpublished trials, which generally were abandoned because of poor recruitment.

Data synthesis

Where the data allowed, the results of comparable groups of trials were pooled using both fixed-effect and random-effects models; the selection of the model for presentation was determined by the consideration of the extent of the heterogeneity.

Subgroup analysis and investigation of heterogeneity

We set out *a priori* two subgroup analyses: by age (primarily, under versus over 65 years) and by types of fracture (primarily, minimally displaced versus displaced, based on the Neer classification). To test whether the subgroups are statistically significantly different from one another, we planned to inspect the overlap of confidence intervals and perform the test for subgroup differences available in Review Manager.

Sensitivity analysis

We planned sensitivity analyses based on aspects of trial and review methodology, including the effects of missing data, the inclusion of studies at high or unclear risk of bias (primarily, selection bias with reference to allocation concealment), the inclusion of studies only reported in abstracts and using fixed-effect versus random-effects models for pooling.

'Summary of findings' tables and quality assessment of the evidence

We produced 'Summary of findings' tables only for the two comparisons where a more substantive body of evidence had accrued. We used the GRADE approach to assess the quality of evidence related to each of the key outcomes listed in the Types of outcome measures for each comparison (see the *Cochrane Handbook for Systematic Reviews of Interventions* Section 12.2, Schunemann 2011).

RESULTS

Description of studies

Results of the search

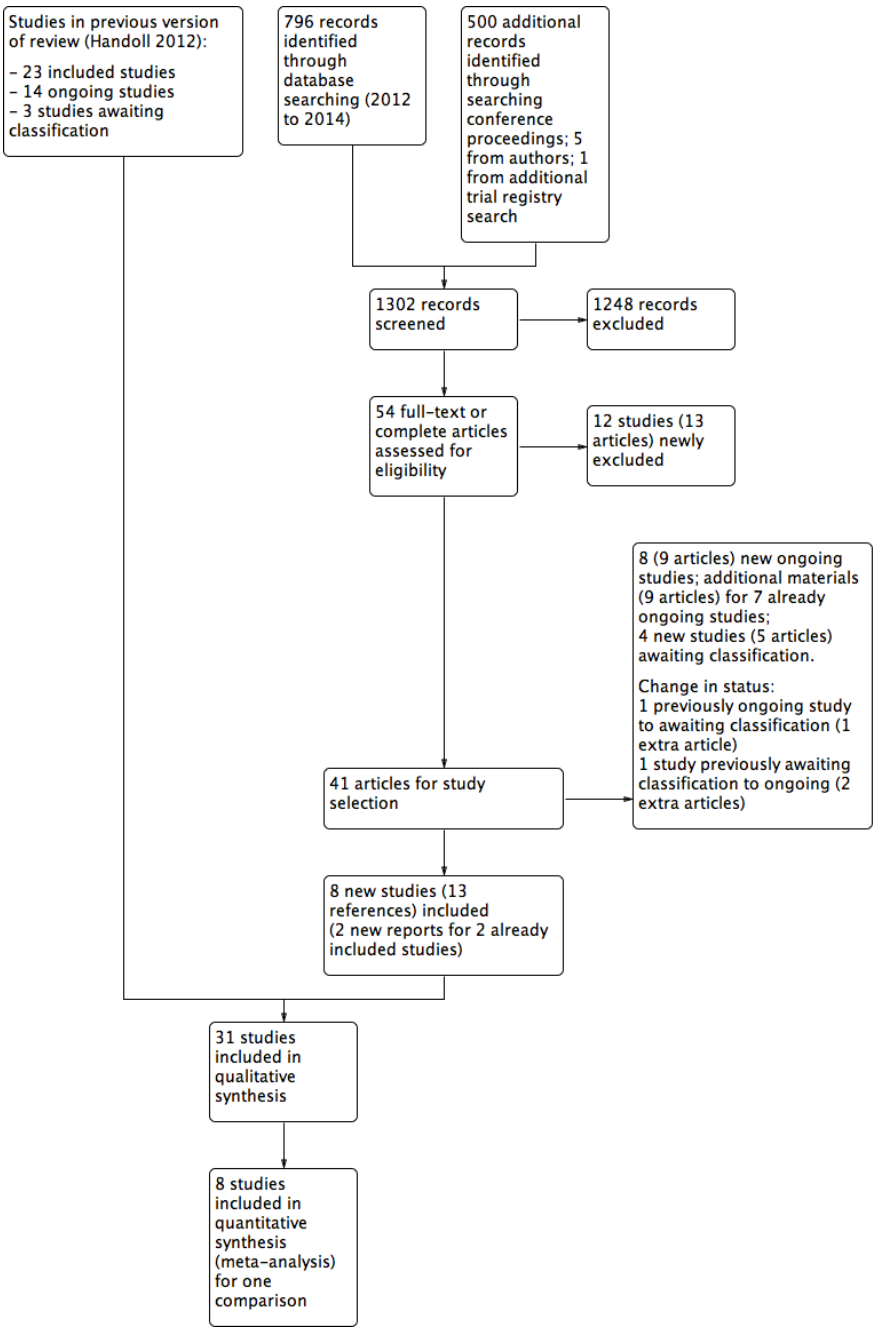
The search was updated from January 2012 to November 2014. We screened a total of 796 records from the following databases: the Cochrane Bone, Joint and Muscle Trauma Group Specialised Register (26), CENTRAL (91), MEDLINE (114), EMBASE (199), CINAHL (129), AMED (5), PEDro (55), WHO Trials Registry (61), ISRCTN registry (66) and ClinicalTrials.gov (50). We also identified four potentially eligible studies from other sources (abstracts of American Academy of Orthopaedic Surgeons annual meeting 2014 (331), the American Orthopaedic Trauma Association annual meetings (2012 to 2014) (96), The Bone and Joint Journal Orthopaedic Proceedings (13); British Elbow and Shoulder Society annual meetings (2011 to 2013) (23), British Trauma Society Annual Scientific Meeting 2014 (37); and reports for three other trials from the review authors (4)). Subsequent notification of an ongoing study was received from a trialist (Torrens). One other ongoing study was identified from a subsequent trials registry search.

Overall, 32 new studies were identified. Of these, eight were included (Boons 2012; Buecking 2014; Cai 2012; Lopiz 2014; ProFHER 2015 (5 references, including 1 trial registration and trial protocol); Sebastiá-Forcada 2014; Soliman 2013 (2 references, including 1 trial registration); Torrens 2012 (1 reference and unpublished data)), 12 were excluded (Cigni 2012; Elidrissi 2013; Erdoğan 2014; Fan 2012; IRCT2013052313435N1; Maniscalco 2014a (2 references); Martetschlager 2012; NCT00384852; NCT01532076; NCT02122315; NTR2186; Zuckerman 2012), eight were placed in ongoing trials (NCT01524965; NCT01847508; NCT01984112; NCT02075476; NTR4019; ROTATE (2 references, including 1 trial registration); SHeRPA; Torrens) and four await classification (Liu 2011 (2 papers); NCT02052206; Wang 2013; Zhu 2014).

Further information was obtained for several studies in the previous version (Handoll 2012); this included the two-year follow-up report (Fjalestad 2014a) of functional outcome for Fjalestad 2010, and an additional article (Ockert 2014), which reported on 48 additional participants for Ockert 2010. A trial registration document and published protocol (Fjalestad 2014b) were found for a newly designated ongoing trial (DELPHI), previously Fjalestad (RCT proposal) in studies awaiting classification. Published protocols were also found for two ongoing trials (HOMERUS (Verbeek 2012); TPHF (Launonen 2012)). Additional information from updated trial registration documentation was added in for seven ongoing trials (HURA; NCT00438633; NCT00818987; NCT00999193; NCT01113411; NCT01557413; TPHF). Ad-

ditional information was also available for Brorson 2009 which was moved from ongoing to studies awaiting classification.
Summaries of the trial populations of past and the present versions of this review as well as the changes between updates are presented in Appendix 2.
In all, 31 trials are now included, 38 trials are excluded, 21 trials are listed as ongoing and seven are in Studies awaiting classification. A flow diagram summarising the study selection process is shown in Figure 1.

Figure 1. 8 (9 articles) new ongoing studies; additional materials (9 articles) for 7 already ongoing studies4 new studies (5 articles) awaiting classificationChange in status:1 previously ongoing study to awaiting classification (1 extra article)1 study previously awaiting classification to ongoing (2 extra articles)Study flow diagram



Included studies

Thirty included trials were published as full reports in journals, their availability ranging from 1979 (Lundberg 1979) to 2015 (ProFHER 2015). The remaining trial was published as a conference abstract only (Torrens 2012). Additional information via other publications, conference abstracts, trial registration details and communications from trial investigators were available for 15 trials (Agorastides 2007; Boons 2012; Fjalestad 2010; Hodgson 2003; Hoellen 1997; Lefevre-Colau 2007; Ockert 2010; Olerud 2011a; Olerud 2011b; ProFHER 2015; Soliman 2013; Torrens 2012; Voigt 2011; Zhang 2011; Zyto 1997); these sometimes preceded the availability of the main report. Details of study methods, participants, interventions and outcome measurement for the individual studies are provided in the Characteristics of included studies and summarised below.

Design

Thirty trials were randomised clinical trials, although seven of these provided no details of their method of randomisation and thus the use of quasi-randomised methods for sequence generation cannot be ruled out (Cai 2012; Hoellen 1997; Kristiansen 1988; Kristiansen 1989; Lundberg 1979; Stableforth 1984; Wirbel 1999). Rommens 1993 was a quasi-randomised trial using alternation for treatment allocation. Livesley 1992 was double-blinded. Of note is that the design of ProFHER 2015, a multicentre trial that compared surgical versus non-surgical treatment, was purposefully pragmatic such as in the requirement for individual surgeons to use surgical methods and implants with which they were familiar.

Sample sizes

The 31 included trials involved a total of 1941 participants. Study size ranged from 20 participants (Bertoft 1984) to 250 participants (ProFHER 2015). One trial (Kristiansen 1989) included one person with bilateral fractures; the treatment allocation for this participant is unclear.

Setting

Thirty of the 31 included trials were single centre studies conducted in 13 different countries: Austria (1 trial); Belgium (1); China (3); Czech Republic (1); Denmark (2); Egypt (1); France (1); Germany (5); The Netherlands (1); Norway (1); Spain (3); Sweden (6) and UK (4). (Though essentially a single centre trial, the interventions in Hodgson 2003 were undertaken at two centres within an NHS Trust in the UK.) The remaining trial was a multicentre trial conducted in the UK (ProFHER 2015). Details of the timing or duration or both of trial recruitment provided for 26 included trials (see the Characteristics of included studies) show Stableforth 1984 to have the earliest start date (1970) and longest period of recruitment (11 years).

Participants

With the exception of one trial (Soliman 2013), the majority of participants in each trial were women (67% to 94% of their trial population). Most participants were aged 60 and above; two trials included a small number of children (Livesley 1992; Wirbel 1999). Seventeen trials set lower age limits. In 10 of these (Boons 2012; Cai 2012; Fialka 2008; Fjalestad 2010; Hodgson 2003; Hoellen 1997; Olerud 2011a; Olerud 2011b; Sebastiá-Forcada 2014; Voigt 2011), the age limit restricted the population to older adults; the most extreme was Sebastiá-Forcada 2014, where only people who were 70 years or over were included. Zyto 1997 specified that participants should be "elderly". Exceptionally, the participants of Soliman 2013 were aged between 45 to 60 years, with the majority (78%) being male.

Five trials included only minimally displaced fractures (Bertoft 1984; Hodgson 2003; Livesley 1992; Lundberg 1979; Revay 1992), whereas 22 selected only people with displaced fractures (Agorastides 2007; Boons 2012; Buecking 2014; Cai 2012; Fialka 2008; Fjalestad 2010; Hoellen 1997; Kristiansen 1988; Lopiz 2014; Ockert 2010; Olerud 2011a; Olerud 2011b; ProFHER 2015; Sebastiá-Forcada 2014; Smejkal 2011; Soliman 2013; Stableforth 1984; Voigt 2011; Wirbel 1999; Zhang 2011; Zhu 2011; Zyto 1997). The majority of fractures were minimally displaced in Kristiansen 1989 and Rommens 1993. Lefevre-Colau 2007 included either minimally displaced or "stable" impacted fractures, the latter included two-part and three-part fractures. Torrens 2012 included either minimally displaced or displaced fractures (two-part or three-part fractures were reported). Fractures were graded using the Neer classification system (Neer 1970) in 28 trials, together with the AO classification system (Muller 1991) in Fialka 2008, Lefevre-Colau 2007 and Smejkal 2011. A modification of the AO classification system was described in Wirbel 1999, and no specific classification system was referred to in the remaining two trials (Bertoft 1984; Rommens 1993).

Interventions

Eleven trials evaluated non-surgical treatment; however, this was post-surgical treatment in two of these. Eight trials compared surgical with non-surgical treatment and 12 compared two methods of surgery. A list of the comparisons, associated trials and numbers of trial participants, grouped according to the main objectives presented in the Objectives is given below.

Methods of non-surgical management (including rehabilitation)

Initial treatment, including immobilisation

- "Immediate" physiotherapy within one week of fracture versus delayed physiotherapy after three weeks of immobilisation in a collar and cuff sling: Hodgson 2003 (86 participants).
- Immobilisation in sling and body bandage for one week versus three weeks: Kristiansen 1989 (85 participants).
- Physiotherapy started within three days of fracture versus delayed physiotherapy after three weeks of immobilisation in a sling: Lefevre-Colau 2007 (74 participants).
- Immobilisation in sling for one week versus four weeks; all followed same "progressive rehabilitation" regimen: Torrens 2012 (42 participants).
- Gilchrist arm sling versus "classic" Desault bandage: Rommens 1993 (28 participants).

Continuing management (rehabilitation) after initial sling immobilisation

- Instructed self-exercise versus conventional physiotherapy: Bertoft 1984 (20 participants); Lundberg 1979 (42 participants).
- Swimming pool treatment plus self-training versus self-training alone: Revay 1992 (48 participants).
- Apparatus supplying pulsed electromagnetic field versus dummy apparatus: Livesley 1992 (48 participants).

Surgical treatment versus non-surgical treatment

The currently available trials fall into three subcategories but are all treated together in Effects of interventions.

Fracture fixation versus non-surgical treatment

- Percutaneous reduction and external fixation versus closed manipulation and sling: Kristiansen 1988 (30 participants).
- Internal fixation using surgical tension band or cerclage wiring versus sling: Zyto 1997 (40 participants; three more were recorded in Tornkvist 1995, another report of Zyto 1997).
- Surgery involving open reduction and fixation with a locking plate and metal cerclages versus non-surgical treatment starting with immobilisation of the injured arm in a modified Velpeau bandage: Fjalestad 2010 (50 participants).
- Surgery involving open reduction and fixation with a PHILOS plate and nonabsorbable sutures versus non-surgical treatment starting with arm immobilisation in a sling: Olerud 2011a (60 participants).

Arthroplasty versus non-surgical treatment

- Hemiarthroplasty using the Neer prosthesis versus closed manipulation and sling: Stableforth 1984 (32 participants).
- Humeral head replacement with the Global Fx prosthesis versus non-surgical treatment starting with arm immobilisation in a sling: Olerud 2011b (55 participants).
- Humeral head replacement with the Global Fx prosthesis versus arm immobiliser alone: Boons 2012 (50 participants)

Surgery (surgeon's choice of method according to their experience) versus non-surgical treatment

- Surgery involving internal fixation (primarily locking plate fixation, most commonly PHILOS plate) or hemiarthroplasty versus sling: ProFHER 2015 (250 participants)

Different methods of surgical management

Comparisons of different categories of surgical intervention

- Open reduction with internal fixation using a locking plate (LPHP or PHILOS) versus a locking nail (PHN): Zhu 2011 (57 participants).
- Open reduction and internal fixation using a PHILOS plate versus the Zifko method of minimally invasive fixation with intramedullary K-wire (Kirschner wire) insertion (distally inserted): Smejkal 2011 (61 participants).
- Hemiarthroplasty using a DuPuy prosthesis versus open reduction and PHILOS plate fixation: Cai 2012 (32 participants)
- Hemiarthroplasty using a Global prothesis versus tension band wiring: Hoellen 1997 (30 participants); an additional nine participants were reported in another report of this trial (Holbein 1999).
- Reverse shoulder arthroplasty using the SMR Reverse prosthesis versus hemiarthroplasty using the SMR Trauma prosthesis: Sebastiá-Forcada 2014 (62 participants).

Comparisons of different methods of performing an intervention in the same category

- Deltoid-split approach versus deltopectoral approach for non-contact bridging plate fixation: Buecking 2014 (120 participants)
- Polyaxial versus monoaxial locking plate fixation. NCB-PH plate versus PHILOS plate: Ockert 2010 (76 participants; 124 in a later report of this trial (Ockert 2014)); and HSP plate versus PHILOS plate: Voigt 2011 (56 participants).
- Open reduction with internal fixation with PHILOS locking plate with or without the use of medial support locking screws: Zhang 2011 (72 participants).

- MultiLoc proximal humeral nail (MPHN) - a straight nail - versus Polarus humeral nail - a curved nail: Lopiz 2014 (54 participants)
- Hemiarthroplasty using an EPOCA prosthesis versus hemiarthroplasty using a HAS prosthesis: Fialka 2008 (40 participants).
- Hemiarthroplasty with tenodesis of the long head of the biceps (LHB) versus hemiarthroplasty with LHB tendon left intact: Soliman 2013 (45 participants)

Continuing management (including rehabilitation) after surgical intervention

- Immobilisation in sling for one week versus three weeks after percutaneous fixation: Wirbel 1999 (77 participants).
- Early active-assisted mobilisation (after two weeks) versus late mobilisation (after six weeks) after cemented hemiarthroplasty: Agorastides 2007 (59 participants).

Outcomes

Many trials in previous versions of this review preceded the availability of validated patient-reported outcome measures (e.g. DASH, Oxford Shoulder Score (Dawson 1996)) for assessing function. From the 2012 update of this review (Handoll 2012), data for these types of outcome have become available from a growing number of trials (Boons 2012; Cai 2012; Fjalestad 2010; Olerud 2011a; Olerud 2011b; ProFHER 2015; Sebastiá-Forcada 2014; Voigt 2011). All trials except Ockert 2010 assessed functioning and pain, but often reported these as part of a combined overall assessment, such as that of Neer (Neer 1970) and Constant (Constant 1987), that included other measures. Most trials reported on adverse events or complications. Exceptionally, Fjalestad 2010 and ProFHER 2015 reported on costs. Livesley 1992 did not provide outcomes split by treatment group.

Excluded studies

Brief details and reasons for exclusion for 26 studies are given in the Characteristics of excluded studies. It is noteworthy that 11 excluded studies were trials that were registered (usually in the now archived National Research Register, UK) but either did not take place (Mechlenburg 2009) or were abandoned due to lack of or poor recruitment (Brownson 2001; Dias 2001; Flannery 2006; Hems 2000; Sinopidis 2010; Wallace 2000; Welsh 2000) or perhaps both of these (Pullen 2007); or not put forward for publication due to compromised methods or data (Bing 2002; Martin 2000). Edelson 2008 also reported an abandoned randomised trial because of lack of patient consent.

Ongoing studies

Details of the 21 ongoing trials are given in the Characteristics of ongoing studies. Two trials, both with three interventions under test, appear in two comparisons (NCT00999193; TPHF). Just two trials (aim 140 participants in total) compare different interventions, early versus late mobilisation or physiotherapy, for non-surgically treated patients (NCT00438633; Torrens). There are four trials (aim 580 participants in total) comparing surgical versus non-surgical treatment; three are multicentre trials (NCT00818987; ProCon; TPHF) and one is a single-centre trial (NCT00999193). Three trials (aim 248 participants in total) are comparing nailing versus plating (NCT01557413; NCT01984112; NTR4019); three trials (aim approximately 385 participants in total) are comparing hemiarthroplasty versus plating (NCT00999193; HOMERUS; TPHF); one trial (aim 120 participants) is comparing reverse shoulder arthroplasty versus plating (DELPHI); and three trials (aim 142 participants in total) are comparing reverse shoulder arthroplasty versus hemiarthroplasty (NCT02075476; NTR3208; SHeRPA). Four trials are comparing different methods of performing an intervention in the same category of which two trials (aim 180 participants in total) are comparing minimally invasive versus usual methods of locking plate fixation (ACTRN12610000730000; HURA), one trial (aim 128 participants) is evaluating screw augmentation of locking plate fixation (NCT01847508) and one trial (aim 40 participants) is comparing two designs of reverse shoulder arthroplasty (NCT01086202). Lastly, two trials (aim 180 participants in total) are evaluating early versus standard rehabilitation after locking plate fixation (NCT01113411; NCT01524965) and one trial is comparing an external rotation brace versus a polysling with the arm in internal rotation (ROTATE).

Studies awaiting classification

Seven studies await classification (see the Characteristics of studies awaiting classification). There are insufficient data for Battistella 2011, reported in a conference abstract only. Brorson 2009, which was listed as ongoing in the 2012 version of the review was stopped after recruiting 25 participants; the use of these data is under discussion. Requests for clarification on study design have been sent to the contact authors of three trials testing bone grafts or substitutes (Liu 2011; Wang 2013; Zhu 2014). The full report of Luo 2008, which tests acupuncture and reports limited findings at one month follow-up, is in Chinese and we will seek translation of this article for a future update. NCT02052206, which is an ongoing trial, also includes patients with osteoarthritis.

New studies found at this update

Eight trials, including a total of 601 participants, were newly included in this update. One trial compared different methods of non-surgical treatment (Torrens 2012); two trials compared surgical with non-surgical treatment (Boons 2012; ProFHER 2015),

and the other five trials compared different methods of surgery (Buecking 2014; Cai 2012; Lopiz 2014; Sebastiá-Forcada 2014; Soliman 2013).

Risk of bias in included studies

The risk of bias judgements on nine items for the individual trials are summarised in Figure 2 and described in the risk of bias tables in the Characteristics of included studies. A 'Yes' (+) judgement means that the authors considered there was a low risk of bias associated with the item, whereas a 'No' (-) means that there was a high risk of bias. Frequently assessments resulted in an 'Unclear' (?) verdict; this often reflected a lack of information upon which to judge the item (see Figure 3). However, lack of information on blinding for functional outcomes was always taken to imply that there was no blinding and rated as a 'No'.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

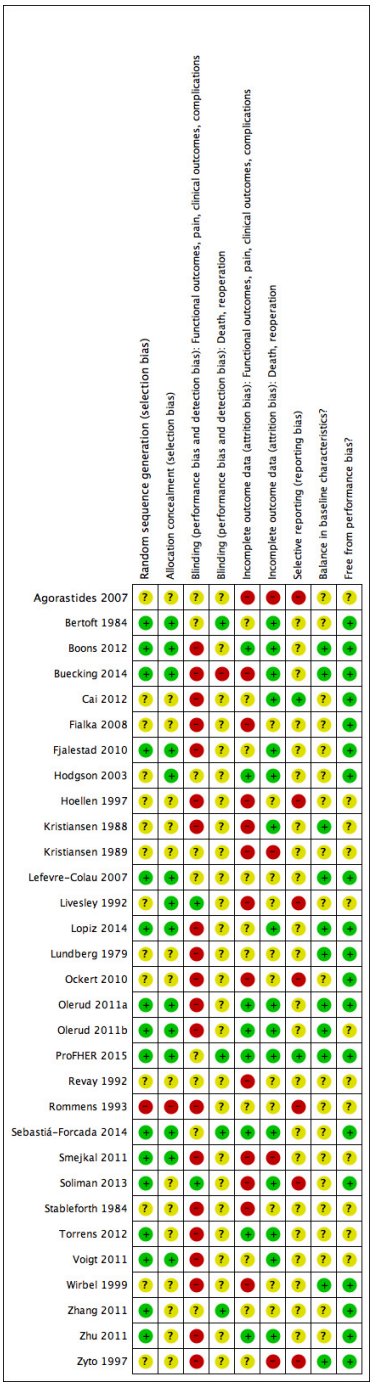
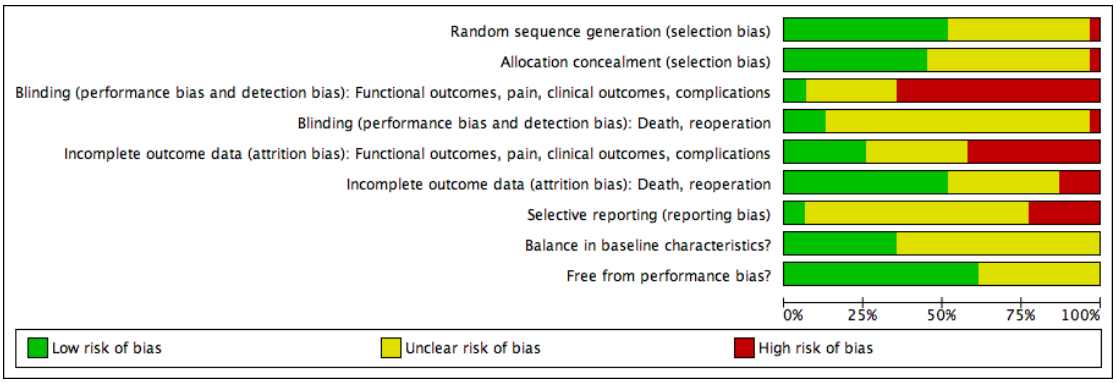


Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Allocation

Twelve trials were judged at low risk of selection bias resulting from adequate sequence generation and allocation concealment (Bertoft 1984; Boons 2012; Buecking 2014; Fjalestad 2010; Lefevre-Colau 2007; Lopiz 2014; Olerud 2011a; Olerud 2011b; ProFHER 2015; Sebastiá-Forcada 2014; Smejkal 2011; Voigt 2011); and a further two trials also took adequate measures to safeguard allocation concealment (Hodgson 2003; Livesley 1992). Based on its post-randomisation application of exclusion criteria, Ockert 2010 was judged at high risk of selection bias; as was Rommens 1993, which was a quasi-randomised trial using alternation.

Blinding

A low risk of detection bias for functional outcomes resulting from assessor and participant blinding was judged for Livesley 1992, which used sham controls, and Soliman 2013, where the intervention was very likely to have remained unknown to the blinded assessor of Constant scores. While several other trials reported blinded assessors, the lack of reporting of adequate safeguards and the lack of blinding of participants or care providers meant that the risk of bias was considered unclear. A high risk of bias reflecting no reporting or indication of blinding was likely in 21 trials. Exceptionally, ProFHER 2015, which did not blind trial participants, personnel or outcome assessment, was rated at 'unclear' risk of bias. This is because statistical tests showed a lack of a significant effect of baseline patient preferences on the primary outcome results (Oxford Shoulder Score).

Incomplete outcome data

Eight trials were considered to be at low risk of bias from the incompleteness of data on functional outcomes (Boons 2012; Hodgson 2003; Olerud 2011a; Olerud 2011b; ProFHER 2015; Sebastiá-Forcada 2014; Torrens 2012; Zhu 2011). Thirteen trials were deemed at high risk of bias, usually reflecting large losses to follow-up and post-randomisation exclusions.

Selective reporting

The lack of trial registration details and protocols hindered the appraisal of the risk of bias from selective reporting. Seven trials were considered at high risk of selective reporting bias (Agorastides 2007; Hoellen 1997; Livesley 1992; Ockert 2010; Rommens 1993; Soliman 2013; Zyto 1997).

Other potential sources of bias

Baseline characteristics

No trial was considered at high risk of bias because of confounding resulting from major imbalances in baseline characteristics. However, low risk of bias judgements were given for only 11 trials (Boons 2012; Buecking 2014; Kristiansen 1988; Lefevre-Colau 2007; Lopiz 2014; Lundberg 1979; Olerud 2011a; Olerud 2011b; ProFHER 2015; Wirbel 1999; Zyto 1997).

Care programmes

Risk of performance bias from important differences in care programmes other than the trial interventions, or differences in the experience of care providers, was judged either low (19 trials) or unclear (in the other 12 trials), usually based on inadequate information.

Effects of interventions

See: **Summary of findings for the main comparison** Summary of findings: surgical versus non-surgical treatment for proximal humeral fractures; **Summary of findings 2** Summary of findings: early versus delayed mobilisation for non-surgically treated proximal humeral fractures

Where available, outcome data reported at final follow-up for individual trials are presented in the analyses.

We based our judgement of clinically important between-group mean differences in the various patient-reported outcome measures (PROMS) using the following minimal clinically important differences (MCID); alternative sources and values are listed in the Primary outcomes. We decided that we would rescale MCIDs where a scoring system was rescaled but would not use these where the scoring instruments were modified, such as question removal.

- ASES (0 to 100: best outcome): 12.01 (Tashjian 2010; rotator cuff disease)
- Constant score (0 to 100: best outcome): 11.6 (Van de Water 2014; proximal humerus fracture)
- DASH (0 to 100: worst outcome): 13.0 (Van de Water 2014; proximal humerus fracture)
- EQ-5D (0 to 1: best outcome): 0.12 (Olerud 2011c; proximal humerus fracture)
- OSS (0 to 48: best outcome): 11.4 (Van de Water 2014; proximal humerus fracture)
- QuickDASH (0 to 100: worst outcome): 16 (DASH/QuickDASH; general)
- SF-12-PCS (physical component score) (0 to 100: best outcome): 6.5 (Schmitt 2004; upper limb proximal diagnosis)
- SST (0 to 12: best outcome): 2.05 (Tashjian 2010; rotator cuff disease)
- UCLA (2 to 35: best outcome): 2.4 (Van de Water 2014; proximal humerus fracture)

Methods of non-surgical management

Initial treatment, including immobilisation

Five trials reported outcomes following initial treatment for non-surgically managed proximal humeral fractures (Hodgson 2003; Kristiansen 1989; Lefevre-Colau 2007; Rommens 1993; Torrens 2012). All or most fractures were described as minimally displaced in three of these trials (Hodgson 2003; Kristiansen 1989; Rommens 1993). Both Lefevre-Colau 2007 and Torrens 2012 included displaced (two- or three-part) fractures; these were described as "stable" in Lefevre-Colau 2007 while Torrens 2012 put an upper limit to fracture displacement.

Early mobilisation versus delayed mobilisation

Although four trials compared early versus delayed mobilisation (Hodgson 2003; Kristiansen 1989; Lefevre-Colau 2007; Torrens 2012), the timing of the start of early mobilisation varied as, where described, did the nature and intensity of the physiotherapy provided. Notable is the long (two hour) duration of individual physiotherapy sessions of Lefevre-Colau 2007. With three exceptions, the lack of comparable outcome measurement and data precluded data pooling and so the results of the individual trials are presented separately below.

Hodgson 2003 compared commencing physiotherapy within one week of fracture versus delayed physiotherapy after three weeks of immobilisation in a collar and cuff sling in 86 people with minimally displaced fractures. The results, presented in Hodgson 2007 for self-reported shoulder disability using the Croft Shoulder Disability Questionnaire (Croft 1994), show a tendency for less disability in the early mobilisation group at one year (e.g. disability (1 or more problems): 18/42 versus 29/40; RR 0.59, 95% CI 0.40 to 0.88; severe disability (5 or more problems): 13/42 versus 17/40; RR 0.73, 95% CI 0.41 to 1.30), continuing improvement and recovery between one and two years, and also reveal that, overall, a substantial proportion of participants continued to report some or severe disability at two years (see Analysis 1.1). Results at two years for eight of the 22 questions of the Croft questionnaire are shown in Analysis 1.2. These are presented to give an indication of the variety of problems experienced by these patients and the variation in the responses. There was some evidence supporting a quicker recovery in the early group as trial participants given early physiotherapy attended fewer treatment sessions (see Analysis 1.3: mean difference (MD) -5.00 sessions; 95% (CI) -8.25 to -1.75) until they and their physiotherapists agreed that independent shoulder function had been achieved. As can be seen in Analysis 1.4, participants of the early group had significantly better health-related quality-of-life scores at 16 weeks in two dimensions of the SF36 (role limitation physical: MD 22.20, 95% CI 3.82 to 40.58; and pain: MD 12.10, 95% CI 3.26 to 20.94). There were no statistically significant differences between the two treatment groups in the other six dimensions (e.g. physical functioning) of the SF36 at 16 weeks, and in all eight dimensions at one year. There were no complications arising from fracture displacement. The only recorded complication in the trial was a frozen shoulder in a participant of the delayed physiotherapy group (see Analysis 1.6). Shoulder function, relative to the unaffected shoulder, measured using the Constant score (Constant 1987) was better at 8 and 16 weeks in the early group (see Analysis 1.8: mean difference in ratio affected/unaffected arm 0.16; 95% CI 0.07 to 0.25). The between-group differences were smaller at one year and the confidence

intervals crossed the line of no effect (MD 0.07, 95% CI -0.03 to 0.17).

Kristiansen 1989, which tested the duration of immobilisation in a sling and body bandage (one week versus three weeks) in 85 people with mainly undisplaced fractures, provided insufficient follow-up data to allow any test for statistical significance. The authors reported that while pain, function and mobility at six months and over were similar in both groups, the patients who started early mobilisation at one week suffered less pain in the first three months than those who kept their bandaging for three weeks. One case of complex regional pain syndrome type 1 (CRPS-1) occurred in each group (see Analysis 1.6).

Lefevre-Colau 2007 compared commencing physiotherapy within three days of fracture with delayed physiotherapy after three weeks of immobilisation in a sling in 74 people with minimally displaced or "stable" impacted fractures. Ten trial participants withdrew from the trial because of difficulties in reaching the hospital for treatment. Participants were discharged from physiotherapy at six months. Shoulder function measured using the Constant score was statistically significantly better in the early group at six weeks and three months (see Analysis 1.9), with the differences probably including a clinically relevant effect; the differences at six months and end of treatment, though favouring the early group, were smaller and not statistically significant (MD 6.10, 95% CI -0.22 to 12.42). Although the early group had significantly reduced pain compared with the three weeks group by three months follow-up, there was no difference at six months (see Analysis 1.11). Active range of motion, measured relative to the opposite arm, also did not differ significantly between the two groups at six months (see Analysis 1.12). There were no cases of fracture non-union or displacement. One participant from each group received treatment for subacromial impingement (see Analysis 1.6). All participants attended at least 70% of the supervised physiotherapy sessions; and very few expressed dissatisfaction with their treatment (see Analysis 1.13).

Torrens 2012 compared sling immobilisation for one week versus four weeks in 42 people with minimally displaced or displaced two- or three-part fractures; all participants had the same "progressive rehabilitation" regimen. Results were reported at 3, 6 and 12 months. Participants in the four-weeks group had consistently higher quality-of-life scores (EuroQol 5D) at all three follow-ups (e.g. MD -0.09, 95% CI -0.21 to 0.03; see Analysis 1.5). All three results include a clinically important difference in quality of life in favour of the four-weeks group but also the possibility of a much smaller and clinically unimportant effect favouring the early group. Torrens 2012 reported no complications aside from noting that the three participants (two early mobilisation versus one, four-weeks immobilisation) experiencing a "significant displacement" of their fracture did not require surgical treatment (see Analysis 1.6). One person had died in the four-weeks group by 12 months follow-up (see Analysis 1.7). The evidence from Torrens 2012 did not confirm differences between the two groups at any of the three follow-ups in Constant scores (see Analysis 1.9), pain (see Analysis 1.10) or patient satisfaction (see Analysis 1.14). Of note though is that the confidence intervals of the pain score results at 12 months included a clinically important difference in favour of the four-weeks group (MD 10.80, 95% CI -4.59 to 26.19); these also crossed the line of no effect.

The exceptions in terms of pooling were data for the adverse events, when pooled under 'shoulder complications' and 'fracture complications', for four and two trials respectively, and the secondary outcomes of pain and Constant scores available from two trials. Data pooled for reported shoulder complications that comprised frozen shoulder, CRPS-1 and treated subacromial impingement showed little difference between the two groups (2/127 versus 3/132; RR 0.73, 95% CI 0.15 to 3.63; 4 trials, 259 participants). Two trials reporting on fracture complications found no cases of non-union and only one trial (Torrens 2012) reported actual cases of fracture displacement (2/52 versus 1/54; RR 2.20, 95% CI 0.22 to 22.45; 2 trials; 106 participants). Both analyses of Constant score and pain (see Analysis 1.9; Analysis 1.10) display evidence of statistical heterogeneity, which may in part reflect clinical heterogeneity of the contributing trials (Lefevre-Colau 2007; Torrens 2012).

Gilchrist arm sling versus the Desault bandage

Rommens 1993 compared the use of two types of immobilisation, the Gilchrist arm sling versus the Desault bandage, worn for two to three weeks in 28 patients with mainly minimally displaced fractures. Reporting up until fracture consolidation, Rommens 1993 reported, without presenting data, that they had found no differences in the end result, either in terms of functional outcome or fracture healing. More people found the initial application of a Desault bandage uncomfortable and severe skin irritation prompted premature removal of the bandage in two people in this group (see Analysis 2.1). Pain during immobilisation was also reported to be greater in the Desault group. Slight displacement of the fracture in the first week was reported in two participants of the Gilchrist group (see Analysis 2.2). At fracture consolidation, patients' rating of their assigned bandage was significantly more favourable in the Gilchrist group (see Analysis 2.3 "Poor or bad rating by patient at fracture consolidation": 2/14 versus 8/14; risk ratio (RR) 0.25, 95% CI 0.06 to 0.97).

Continuing management (rehabilitation) after initial sling immobilisation

Two small trials (Bertoft 1984; Lundberg 1979) compared self-directed exercise following a course of instruction versus conventional physiotherapy during the 12 weeks following trauma in a total of 62 patients with minimally displaced fractures. In both trials there were no statistically significant differences between those receiving instruction for exercises at home and those undergoing

supervised physiotherapy in any of the outcomes recorded (see Analysis 3.1, Analysis 3.2, Analysis 3.3, Analysis 3.4, Analysis 3.5 and Analysis 3.6). It should be noted that since Lundberg 1979 did not report whether there had been any loss to long-term follow-up at an average of 16 months, the results for Neer's score presented in Analysis 3.5 are for illustrative purposes only.

Revay 1992, which included 48 participants with minimally displaced fractures, reported that the addition of supervised exercises in a swimming pool to self-treatment did not enhance long term outcome. Participants of the control group (self-treatment only) were reported as having significantly better functional movements, joint mobility and activities of daily living at two and three month follow-up. However, there were no significant differences at one year. Revay 1992 suggested that those using the pool may have neglected their home exercises, but the authors did not evaluate compliance.

Livesley 1992, which included 48 patients with minimally displaced fractures, reported that there was no difference in outcome between the two groups (pulsed electromagnetic high frequency energy (PHFE) versus placebo) at any stage of the trial, but provided no quantitative data. All trial participants were reported as achieving a "good" result as converse to a "poor" one.

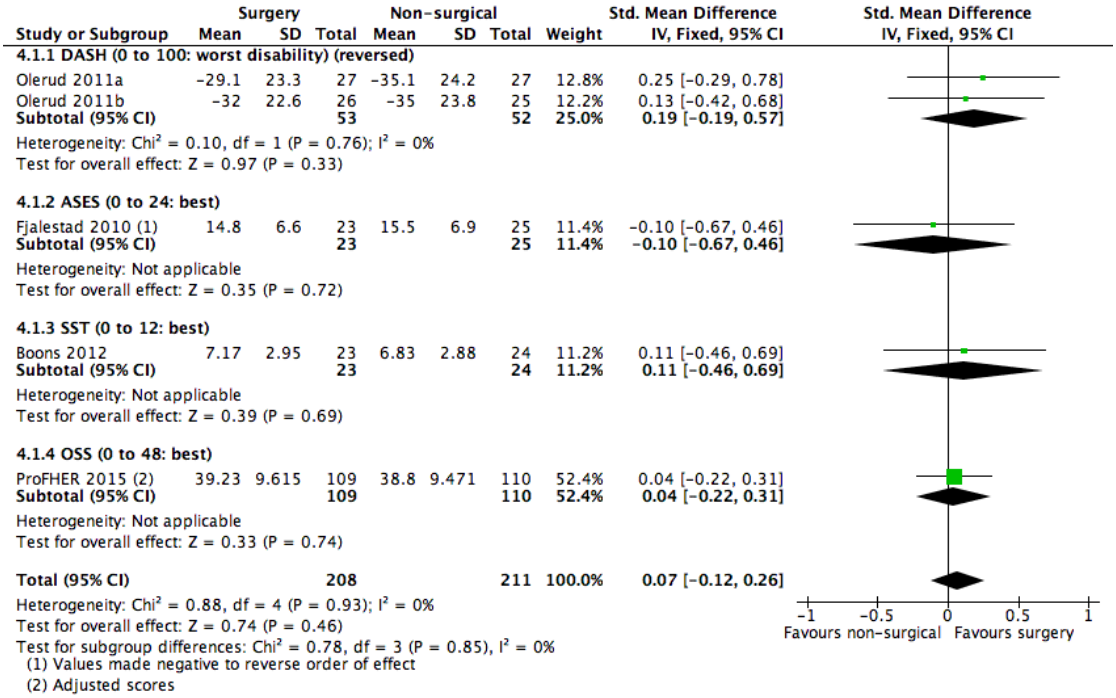
Surgical treatment versus non-surgical treatment

Eight heterogeneous trials, with a total of 567 participants and 568 fractures, evaluated surgical intervention for displaced fractures, of which over 73% were three- or four-part fractures (Neer classification). Table 1 gives a brief summary of their characteristics. The methods of surgery varied between the trials, being restricted to hemiarthroplasty in three trials (Boons 2012; Olerud 2011b; Stableforth 1984), internal fixation in three trials (Fjalestad 2010; Olerud 2011a; Zyto 1997) and external fixation in Kristiansen 1988. Most surgery involved internal fixation in ProFHER 2015, where the surgeons used methods with which they were experienced. Non-surgical treatment was predominantly sling immobilisation; this was preceded by closed manipulation in all participants in two trials (Kristiansen 1988; Stableforth 1984) and in eight participants in Fjalestad 2010.

Primary outcomes

Pooled results of four different patient-reported functional scores reported by five trials (Boons 2012; Fjalestad 2010; Olerud 2011a; Olerud 2011b; ProFHER 2015) at 12 months follow-up showed no statistically significant difference between the two groups (standardised mean difference (SMD) 0.07 favouring surgery, 95% CI -0.12 to 0.26; P = 0.46; 419 participants, see Analysis 4.1; and Figure 4). The same finding, which was based on data for three scores reported by four trials, of no significant between-group difference applied at 24 months (SMD 0.07 favouring surgery, 95% CI -0.14 to 0.28; P = 0.50; 351 participants; see Analysis 4.2). The Oxford Shoulder Score (OSS) results for ProFHER 2015 showed no clinically important (the MCID for the OSS was set at 5 points in this trial) or statistically significant differences between the two groups over the two-year follow-up (MD 0.75, 95% CI -1.68 to 3.18; P = 0.55; 231 participants) or at 6, 12 or 24 months (see Analysis 4.3). Pooled DASH scores from Olerud 2011a and Olerud 2011b showed no statistically significant differences between the two groups at four months, or at one or two years (see Analysis 4.4); although the scores favoured surgery, the best estimate at 24 months was still lower than the MCID (10 points) for DASH (0 to 100: worst function): MD -7.43, 95% CI -16.26 to 1.41; 99 participants). Fjalestad 2010 found no significant differences between the two groups in the American Shoulder and Elbow Surgeons (ASES: 0 to 24: best function) scores at either 6, 12 or 24 months follow-up (see Analysis 4.5). Boons 2012 found no significant differences between the two groups in the Simple Shoulder Test scores at 3 or 12 months (see Analysis 4.6). There were no statistically significant differences in subjective assessment of function between the two groups of Zyto 1997 at either one or three years (see Analysis 4.7).

Figure 4. Forest plot of comparison: 4 Surgical versus non-surgical treatment, outcome: 4.1 Functional scores at 12 months (higher = better outcome).



Quality of life based on the EuroQol scores from three trials (Olerud 2011a; Olerud 2011b; ProFHER 2015) and 15D (Sintonen 2001) results from Fjalestad 2010 were slightly higher in the surgery group but none of the between-group differences were clinically important including the statistically significant finding at six months (MD 0.04, 95% CI 0.01 to 0.08; P = 0.02; 381 participants; see Analysis 4.8). A separate breakdown of the results from Fjalestad 2010, which include the number of quality of life years (QALYs), showed no differences in any quality-of-life outcomes for this trial (see Analysis 4.9). Based on data adjusted for covariates, ProFHER 2015 reported there were also no significant between-group differences over two years in the mean SF-12 physical component score (MD 1.77 favouring surgery, 95% CI −0.84 to 4.39 points; reported P = 0.18) and the mean SF-12 mental component score (1.28 favouring non-surgical treatment, 95% CI −3.80 to 1.23; reported P = 0.32). The SF-12 physical component scores (0 to 100: best outcome) were slightly higher in the surgery group at all three follow-ups (see Analysis 4.10) and, conversely, the SF-12 mental component scores (0 to 100: best outcome) were slightly higher in the non-surgical treatment group at all three follow-ups (see Analysis 4.11). None of these differences was statistically significant and the confidence interval limits are less than the minimal clinically important difference.

There was no significant difference between the two groups in mortality (17/248 versus 12/248; RR 1.40 favouring non-surgical treatment, 95% CI 0.69 to 2.83; P = 0.35; 6 trials, see Analysis 4.12). Where reported, none of the deaths was related to their fracture or treatment with the exception of one early death due to venous thromboembolism in the surgical group of ProFHER 2015. Notably, the two deaths that occurred within three months of surgery in Fjalestad 2010 were people with underlying health problems. In Zyto 1997, eight of the 11 missing participants had died at 50 months, but no information on group allocation or causes of death was provided.

Significantly more surgical group patients had additional or secondary surgery (34/262 versus 16/261; RR 2.06, 95% CI 1.18 to 3.60; 7 trials; see Analysis 4.13). In Boons 2012, one surgical group participant underwent revision surgery after one week because of head-stem separation. A non-surgically treated participant in Boons 2012 who had surgery at 13 months, thus outside the trial's follow-up period, because of shoulder pain and impairment was not included in this analysis. In Fjalestad 2010, treatment failure resulting in an operation occurred in eight surgical group participants, one of whom had re-fixation plus bone grafting at six months and seven whose implants were removed because of screw penetration into the joint space; and one non-surgically treated patient, who had surgery because of fracture redisplacement at two

weeks. In Kristiansen 1988, the three cases of treatment failure were the removal of pins due to infection in one surgical group participant and a change of method resulting from a poor initial fracture reduction in two non-surgical group participants. The reasons for re-operations in the surgical group of Olerud 2011a were deep infection (two cases), non-union (one case), impingement (two cases), avascular necrosis (one case), screw penetration into joint (one case) and stiffness (two cases). One non-surgically-treated patient in Olerud 2011a had surgery because of impingement. Not included in this analysis is another non-surgically-treated patient with non-union who abstained from surgery partly because of a late diagnosis of axillary nerve palsy. The reasons for additional surgery in Olerud 2011b were screw penetration of the joint (for one patient treated with a locking plate), stiffness and impingement and displaced greater tuberosity respectively in three surgical group patients, and for complete displacement of the humeral shaft without bony contact in one non-surgically treated patient. Not included in this analysis is another non-surgically-treated patient who refused surgery for a non-union. The reasons for further surgery in the surgical group of ProFHER 2015 were avascular necrosis (two cases), metalwork problems (seven cases) and post-traumatic stiffness (two cases). The reasons for subsequent surgery in the non-surgical treatment group of ProFHER 2015 were avascular necrosis (one case), malunion (two cases), non-union (four cases), post-traumatic stiffness (one case), rotator cuff tear (one case), severe pain (one case) and not-reported (one case). In Stableforth 1984, one surgical group participant had their prosthesis removed because of a deep infection. Only ProFHER 2015 reported on additional shoulder-related therapy, which occurred in slightly more participants of the surgery group (7/125 versus 4/125; RR 1.75 favouring non-surgical treatment, 95% CI 0.53 to 5.83; P = 0.36; see Analysis 4.14).

The numbers of people in each group with one or more adverse events or complications were available only in ProFHER 2015 (30/125 versus 23/125; RR 1.30 favouring non-surgical treatment, 95% CI 0.80 to 2.11; P = 0.28; see Analysis 4.14). Analysis 4.14 also presents the available data for individual complications. Unsurprisingly, surgery-related complications (e.g. infection and screw penetration of the joint) were predominant in the surgery treatment group. While non-union was more common in the non-surgical treatment group (P = 0.05), none of the differences between the two groups in the radiologically detected outcomes of avascular necrosis and signs of osteoarthritis were statistically significant. For avascular necrosis, data favouring surgery from Boons 2012 and Olerud 2011b needs to be seen in the context that these were only likely to be detected in non-surgically treated patients, given that surgery involved the replacement of the humeral head. Additionally, some of these outcomes were without symptoms or minor in extent. For instance, in Fjalestad 2010, both cases of non-union in the non-surgical treatment group were without symptoms, and 22 of the 27 participants with radiographically-detected avascular necrosis were asymptomatic.

In Stableforth 1984, fewer participants of the prosthesis group needed some help with activities of daily living or had died by six months (see Analysis 4.15: 2/16 versus 9/16; RR 0.22, 95% CI 0.06 to 0.87).

Secondary outcomes

The differences between the two groups in the Constant scores (0 to 100: best outcome) at four different time points (3-4, 12, 24 and 50 months) were all small and clinically not important (e.g. the most data were for 12 months: MD 2.81, 95% CI -2.20 to 7.82; 199 participants, 4 trials; see Analysis 4.16). The same lack of differences between the two groups applied to the Constant scores of the injured arm in Fjalestad 2010 at 6, 12 and 24 months follow-up (see Analysis 4.17). At one year follow-up in Kristiansen 1988, fewer participants of the surgical group had a poor or unsatisfactory rating of function assessed using the Neer score (3/11 versus 6/10; RR 0.45, 95% CI 0.15 to 1.35; see Analysis 4.18).

Boons 2012 reported similar results in the two groups for patient-assessed disability based on a 0 to 100 VAS scale; where the maximum score equated to "no restrictions". The clinical relevance of the results, which were in favour of the surgical group, is uncertain (see Analysis 4.19).

Boons 2012 reported lower pain scores, measured using VAS (0 to 100: higher scores mean worse pain), in the hemiarthroplasty group at three months (MD -18.00, 95% CI -29.03 to -6.97; 49 participants; see Analysis 4.20) than in the non-surgical group; this difference is likely to be clinically important. In contrast, there were similar results in the two groups at 12 months (median 23 in the surgery group versus 25 in the non-surgical group; reported P = 0.725). Pooled results from two trials (Olerud 2011a; Olerud 2011b) showed slightly less pain at two year follow-up in the surgery group (MD -6.38; 95% CI -14.18 to 1.41; 101 participants; see Analysis 4.20); the clinical importance of this result is questionable. Nearly all trial participants in Stableforth 1984 had shoulder pain but fewer in the prosthesis group reported constant pain that impaired sleep or function (see Analysis 4.22: 2/15 versus 9/15; RR 0.22, 95% CI 0.06 to 0.86). The categorisation of pain is not clear in the trial report nor whether pain was assessed for all participants. Assuming the latter is the case, the difference between the two groups is less marked when all those with more than occasional pain are included (4/15 versus 9/15; RR 0.44, 95% CI 0.17 to 1.13; analysis not shown). Zyto 1997, which provided a breakdown of the Constant score into the separate components (activities of daily living, pain, range of motion, strength), did not confirm a significant difference between the two groups in the pain component, which was in favour of the non-surgical treatment group, at 50 months (see Analysis 4.21).

Reduced muscle strength and restricted mobility were less frequent in the prosthesis group survivors of Stableforth 1984 (see Analysis 4.23 and Analysis 4.24) than in the group receiving closed manipulation and sling. Zyto 1997 found no difference between the two

groups in strength ('power') at 50 months follow-up. The clinical relevance of the three point difference in the range of motion component of the Constant score in favour of non-surgical treatment is questionable (see Analysis 4.21). In Boons 2012, abductor strength, reported as a percentage of the opposite shoulder, was lower in the surgery group at both three months (median values: 20% versus 30%; reported P = 0.015) and 12 months (median values: 24% versus 42%; reported P = 0.008). Boons 2012 also found that forward flexion (median 68 versus 88 degrees; reported P = 0.001) and abduction (median 61 versus 78 degrees; reported P = 0.02) were worse in the surgery group at three months. There were no between-group differences in external rotation and internal rotation at this time, nor for all four range of motion measures at 12 months).

Fjalestad 2010 found no differences at one year between the two groups in costs (see Analysis 4.25 and Analysis 4.26). The base case economic analysis of ProFHER 2015 showed that at two years, the cost of surgical intervention was, on average, GBP 1,780.73 more per patient (95% CI GBP 1,152.71 to GBP 2,408.75).

Different methods of surgical management

Comparisons of different categories of surgical intervention

Five trials compared different methods of surgical management (Cai 2012; Hoellen 1997; Sebastiá-Forcada 2014; Smejkal 2011; Zhu 2011).

Open reduction with internal fixation using a locking plate versus a locking nail

Zhu 2011 compared open reduction with internal fixation using a locking plate (LPHP or PHILOS) versus a locking nail (PHN) in 57 participants with two-part surgical neck fractures. The American Shoulder and Elbow Surgeon's scores were statistically significantly better in the plate group at one year (MD 7.20; 95% CI 1.48 to 12.92) and three years (MD 4.00; 95% CI 0.01 to 7.99) (see Analysis 5.1). The clinical importance of these findings, however, is uncertain given the MCID for ASES is included only in the 95% CI at one year follow-up. One participant of the nail group died of unrelated causes. While complications were not described in full, significantly more patients in the plate group had a complication (9/29 versus 1/28; RR 8.69, 95% CI 1.18 to 64.19; see Analysis 5.2). This included five patients in the plate group who had a re-operation for screw penetration into the articular surface of the humeral head. Zhu 2011 found a statistically significant but probably not a clinically important difference in favour of the plate group in pain at one year but not at three years (see Analysis 5.3). There were no statistically significant differences between the two groups in the Constant scores at the two follow-up times (see Analysis 5.4) or in range of motion measures at either one year (not shown) or three years (see Analysis 5.5 and Analysis 5.6). Although the plate group had greater muscle strength at one year, the difference between the two groups was no longer statistically significant at three years (see Analysis 5.7). Both duration of surgery (MD 24.90 minutes, 95% CI 5.97 to 43.83 minutes) and blood loss were statistically significantly greater in the plate group (see Analysis 5.8). Consistent with the finding of an increased blood loss in the plate group, more people in this group had a blood transfusion but the difference between the two groups was not statistically significant (see Analysis 5.9).

Open reduction with internal fixation using a locking plate versus minimally invasive fixation with distally inserted intramedullary K-wires

Smejkal 2011 compared open reduction and internal fixation using a PHILOS plate versus the Zifko method of minimally invasive fixation with distally inserted intramedullary K-wires (Kirschner wires) in 61 participants with two- or three-part fractures. Smejkal 2011 did not report patient-reported function or activities of daily living. The account of the complications seemed incomplete, with no indication of how many required a re-operation but this was perhaps partly due to difficulties in translation from Czech to English. There was no significant difference between the two groups in the overall numbers of participants incurring a complication (11/28 versus 9/27; RR 1.18, 95% CI 0.58 to 2.38; see Analysis 6.1 The recorded nature of the complications reflected the type of implant, with four cases of screw protrusion in the plate group that resulted in impingement and migration of K-wires, a distal humeral fracture and a nerve injury in the Zifko group. Smejkal 2011 found no difference between the two groups in Constant scores relative to the healthy limb at a mean two years follow-up (MD -0.81%, 95% CI -7.45% to 5.83%; see Analysis 6.2). Three participants of each group had a 'poor' Constant score. Analysis 6.3 shows there were no statistically significant differences between the two groups in time to union (MD 2.10 weeks, 95% CI -2.25 to 6.45 weeks) or in a vaguely-described measure of time to recover normal upper limb function (27.2 versus 21.4 weeks; MD 5.80 weeks; 95% CI -0.16 to 11.76 weeks). Smejkal 2011 suggested that the greater time to recover in the plate group reflected a greater impact of complications in this group. The duration of operation was significantly greater in the plate group (MD 44.74 minutes, 95% CI 32.23 to 57.25 minutes; see Analysis 6.4), but with a non-significant tendency for less X-ray exposure. The tendency for longer hospital stays for plate group patients did not achieve statistical significance (MD 1.20 days; 95% CI -0.34 to 2.74; see Analysis 6.5).

Hemiarthroplasty versus internal fixation

Two small heterogeneous trials compared humeral head replacement versus internal fixation for four-part fractures (Cai 2012;

Hoellen 1997). Only data for re-operation were available for pooling; these favoured hemiarthroplasty (3/34 versus 8/28; RR 0.32, 95% CI 0.10 to 1.10) but were moderately heterogeneous (heterogeneity: $Chi^2 = 1.82$, degrees of freedom (df) = 1 (P = 0.18); $I^2 = 45\%$; see Analysis 7.3). Given this, the results of the two trials are presented separately.

Hemiarthroplasty versus open reduction and locking plate fixation:

Cai 2012, which compared hemiarthroplasty with open reduction and PHILOS plate fixation in 32 participants with four-part fractures, reported outcome at 4, 12 and 24 months. Although DASH scores at one and two years favoured the hemiarthroplasty group, the mean differences were smaller than the MCID of 13 for DASH (at 12 months: MD -7.30, 95% CI -16.70 to 2.10, 28 participants; at 24 months: MD -6.10, 95% CI -11.03 to -1.17, 27 participants; see Analysis 7.1). Although favouring the hemiarthroplasty group, the differences between the two groups in quality of life measured via the EQ-5D were not clinically or statistically significant at any of the three follow-up times (see Analysis 7.2). Re-operations were reported for three participants in the hemiarthroplasty group (one dislocation, one prosthesis loosening, one infection) and three participants in the fixation group (one non-union, two fixation failure); RR 0.68, 95% CI 0.16 to 2.88; see Analysis 7.3). One person in the hemiarthroplasty group had died by two years (see Analysis 7.4). The Constant scores were higher in the hemiarthroplasty group at all three follow-ups; in particular, the 95% confidence interval at two years included a clinically important effect (MD 12.20, 95% CI 2.85 to 21.55; 27 participants; see Analysis 7.6). While the results at two years for pain and range of motion favoured hemiarthroplasty, Cai 2012 found no statistically significant between-group differences in either of these outcomes (see Analysis 7.7 and Analysis 7.9). The mean time of surgery was slightly longer in the hemiarthroplasty group (93 minutes versus 86 minutes).

Hemiarthroplasty versus tension band wiring

Hoellen 1997 compared hemiarthroplasty versus reduction and stabilisation of the fracture using tension band wiring. All 30 patients reported in Hoellen 1997 had four-part fractures. Patients with three-part fractures were also eligible according to a later report of the trial (Holbein 1999), which reported on 39 patients. However, until we obtain further information from the trialists, we will continue to report the results from Hoellen 1997. In Hoellen 1997, results for only 18 of the 30 trial participants were available at one year. There were no serious peri-operative or post-operative complications such as pulmonary embolism. No participants of the replacement group required further surgery compared with five participants of the osteosynthesis group (the wires displaced in four participants and the fracture completely dislocated in one participant): RR 0.09, 95% CI 0.01 to 1.51 (see Analysis 7.3). Implants were removed in four participants of the osteosynthesis group (see Analysis 7.5). The mean Constant scores (minus the power component) for the 18 people available at one year follow-up were similar in the two groups (48 versus 49 points out of a maximum of 75). Two participants of the hemiarthroplasty group and one in the fixation group reported pain at one year (see Analysis 7.8). Though we have not obtained clarification on the inadequately reported results presented in Holbein 1999, these did not appear to differ in a major way from those in Hoellen 1997.

Reverse shoulder arthroplasty versus hemiarthroplasty

Sebastiá-Forcada 2014 compared reverse shoulder arthroplasty with hemiarthroplasty in 62 participants with either three- or four-part fractures, some of which included dislocation. Follow-up was between 24 and 49 months. Patient-reported upper-limb function pain assessed using the Quick DASH (0 to 55: worst outcome) was superior in the reverse arthroplasty group: MD -6.90, 95% CI -10.81 to -2.99 (see Analysis 8.1). One participant in the reverse arthroplasty group was re-operated because of deep infection compared with six participants in the hemiarthroplasty group re-operated because of proximal migration of implant (1/31 versus 6/31; RR 0.17 favouring reverse arthroplasty, 95% CI 0.02 to 1.30; see Analysis 8.2). All seven participants received a reverse shoulder arthroplasty. No deaths occurred in this trial. University of California-Los Angeles scores and Constant and adjusted Constant scores all favoured the reverse arthroplasty group (see Analysis 8.4). A similar finding applied to pain, range of motion, power and activities of daily living components of the Constant score (see Analysis 8.5). Fewer participants had a complication in the reverse arthroplasty group compared with the hemiarthroplasty group (2/31 versus 10/30; RR 0.19, 95% CI 0.05 to 0.81; see Analysis 8.6 footnotes for actions taken to treat the individual complications). The findings of radiological assessment (see Analysis 8.7) did not confirm a difference between the two groups in malunion or resorption of tuberosities. The one case of scapular notching in the reverse arthroplasty group was without clinical consequence, as were the 11 cases of heterotopic ossification. Anterior forward and abduction were superior in the reverse arthroplasty group (Analysis 8.8).

Comparisons of different methods of performing an intervention in the same category

Seven trials compared different types or methods in the same intervention category (e.g. plating) (Buecking 2014; Fialka 2008; Lopiz 2014; Ockert 2010; Soliman 2013; Voigt 2011; Zhang 2011).

Deltoid-split approach versus deltopectoral approach for non-contact bridging plate fixation

Buecking 2014, which made this comparison in 120 people with Neer two-, three- or four-part fractures, reported results for activity of daily living at 6 and 12 months based on a score by Lawton (Lawton 1969). However, the trialists appear not to have used the scoring system correctly and reported scores that are greater than the maximum score of 8. There was no statistically significant difference between the mean scores at six months or 12 months (18 for the deltoid-split versus 17 for the deltopectoral) but the clinical relevance of these scores is questionable. Similar numbers of participants in the two groups had a re-operation for a complication or a fall (9/60 versus 8/60; RR 1.13, 95% CI 0.47 to 2.72; see Analysis 9.1); the same observation applies to the numbers of participants requesting plate removal (see Analysis 9.1). By one year follow-up, one person had died in the deltoid-split group versus three in the deltopectoral group (see Analysis 9.2). Analysis 9.3 presents the data for the complications, all present resulted in a re-operation, reported for this trial. The Constant scores favoured the deltoid-split group, but the mean differences were smaller than the MCID for the Constant score and the confidence intervals crossed the line of no effect (see Analysis 9.4). A similar finding applied to the pain VAS results (see Analysis 9.5). There were no significant between-group differences in duration of operation or fluoroscopy time (see Analysis 9.6). The mean length of stay in hospital was 10 days in both groups (see Analysis 9.7).

Polyaxial versus monoaxial locking plate fixation

Two trials made this comparison (Ockert 2010; Voigt 2011). Ockert 2010, which reported on outcome for patients (66 patients in their 2010 publication; 124 patients in their later publication (Ockert 2014)) with Neer two-, three- or four-part fractures, did not report on functional outcome. Voigt 2011 found no statistically significant differences at one year (48 patients with Neer three- or four-part fractures) between the two groups in their DASH scores (see Analysis 10.1: RR 2.10, 95 CI -6.24 to 10.44), nor at 3, 6 or 12 months in the 'simple shoulder test' (see Analysis 10.2).

Since the extended trial report of Ockert 2010 (Ockert 2014) reported only on re-operation at 12 months, the data from the more detailed report of re-operations and complications occurring up to six months from the 2010 publication are also presented in the following. Neither trial found statistically significant differences between the two groups in participants having a re-operation; either at six months (data from Ockert 2010: 2/29 versus 3/37) or at one year (see Analysis 10.3: 15/83 versus 16/97; RR 1.10, 95% CI 0.58 to 2.08). In the initial six months follow-up report for Ockert 2010, one participant of the polyaxial group had a loosened screw taken out at 10 weeks; one participant of each group had early hardware removal (at five months) because of subacromial impingement from poor plate positioning; and two monoaxial group participants had early hardware removal and a revision respectively because of intra-articular screw protrusion. In the recruitment and follow-up extension of Ockert 2010 (Ockert 2014), five polyaxial group versus nine monaxial group participants had revision because of secondary varus displacement with subsequent intra-articular screw protrusion; four versus two participants had revision because of subacromial impingement; and one monoaxial group participant had revision surgery because of an infection. In Voigt 2011, one person in each group had an early "prosthetic replacement" and three participants in the polyaxial group and one in the monoaxial group had refixation. The two other re-operated polyaxial group participants of Voigt 2011 had a corrective osteotomy and a screw removal respectively, while two other re-operated monoaxial group participants both had early implant removals.

Similarly, neither trial found statistically significant differences between the two groups in their other reported outcome measures. The available data are shown for death (see Analysis 10.4), participants with any or individual complications (see Analysis 10.6), the Constant score relative to the uninjured arm (see Analysis 10.5), range of motion (see Analysis 10.7) or duration of operation or fluoroscopy time (see Analysis 10.8).

Locking plate: use of medial support locking screws

Zhang 2011 tested the use of the medial support locking screws in 72 people with Neer two-, three- or four-part fractures treated with open reduction with internal fixation using the PHILOS locking plate. They reported results for 68 participants. In the medial support group, locking screws were introduced through the plate so as to run up the inferior portion of the humeral neck providing support to the calcar. In the control group, these screw holes were left empty. One participant in the medial screw group had early failure of fixation due to plate breakage compared with nine participants with early fixation failure (six varus collapse; three screw penetration) in the control group; however, this difference did not reach statistical significance (see Analysis 11.1: RR 0.15, 95% CI 0.02 to 1.11). Seven of these patients, including the patient in the medial screw group, consented to have a re-operation (RR 0.22; 95% CI 0.03 to 1.11). One patient in the medial screw group had asymptomatic osteonecrosis. The medial screw group had statistically significantly higher Constant scores (0 to 100: best score) at 31 month follow-up (see Analysis 11.2: MD 9.00, 95% CI 2.41 to 15.59).

MultiLoc proximal humeral nail (MPHN) - a straight nail - versus Polarus humeral nail - a curved nail

Lopiz 2014 compared these two types of intramedullary nails in 54 people with Neer two- or three-part fractures, reporting results at a mean of 14 months (range 6 to 22 months). Of the two excluded participants, who were both in the MPHN group, one had died

and one was lost to follow-up. Patient-reported outcome measures were not reported in this trial. Adverse events including re-operations are presented in Analysis 12.1. Significantly fewer participants in the MPHN group had a re-operation (3/26 versus 11/26; RR 0.27 favouring MPHN, 95% CI 0.09 to 0.87; P = 0.03). All re-operations involved hardware removal of either a loose screw (one versus seven) or the whole nail (two versus four). One participant of the Polarus group had a non-union; subsequent to nail removal, this patient had a reverse shoulder arthroplasty. Fewer participants in the MPHN group had rotator cuff symptoms (9/26 versus 19/26; RR 0.47, 95% CI 0.27 to 0.84) or shoulder impingement (2/26 versus 5/26; RR 0.40, 95% CI 0.09 to 1.88). Both the unadjusted and age- and sex-adjusted Constant scores were higher in the MPHN group; e.g. adjusted Constant score: MD 10.60, 95% CI 1.71 to 19.49; Analysis 12.2). Although the MDs were a little smaller than the MCID (11.2) for the Constant score, the 95% confidence intervals included a clinically relevant difference in favour of the MPHN. There were no significant between-group differences in range of shoulder motion (see Analysis 12.3), length of surgery or length of hospital stay (see Analysis 12.4).

Hemiarthroplasty: comparison of two types

Fialka 2008 compared two types of hemiarthroplasty, the EPOCA prosthesis versus the HAS prosthesis, which differ in a number of ways including the method of fixation of the tuberosities. Fialka 2008 reported results at one year for 35 of the 40 trial participants. The treatment allocations of three participants who had died and the two who were lost to follow-up were not reported. Significantly better functional results, including range of motion, at one year were reported for the EPOCA prosthesis group. The relative (compared with the patient's uninjured shoulder) individual Constant score results were 70.4% (range 38% to 102%) for the EPOCA group versus 46.2% (range 15% to 80%) for the HAS group (reported P = 0.001). Reported complications were two patients with deep infection in the EPOCA group, two patients with persistent pain scheduled for a reoperation in the HAS group (see Analysis 13.1), and a periprosthetic fracture that occurred in one of the three patients who had died by one year. Radiological findings, except for heterotopic ossification where there were contradictory data, are shown in Analysis 13.2. These tended to favour the EPOCA prosthesis. Fialka 2008 noted some association between the bony resorption of the tuberosities and a decreased Constant outcome score. Results for range of motion are shown in Analysis 13.3.

Hemiarthroplasty: tenodesis of the long head of the biceps (LHB) versus LHB tendon left intact

Soliman 2013 compared tenodesis of the LHB versus leaving the LHB tendon intact in 45 people undergoing hemiarthroplasty. By deduction from the study report, four participants in each group were excluded because they had a complication within three months of follow-up. These were reported to be tuberosity malposition (three participants); inferior subluxation of the prosthesis (two participants), loss of reduction of the greater tuberosity (two participants) and deep infection that required surgical debridement (one participant). Data for complications split by treatment group are shown in Analysis 14.1. Of these complications, only deep infection resulted in further surgery. At two years, the difference between the two groups in the Constant scores in favour of the tenodesis group was below the MCID and thus unlikely to be clinically important (MD 4.60, 95% CI 0.38 to 8.82; see Analysis 14.2). Three participants reported mild pain in the tenodesis group and six participants reported pain (four mild and two moderate pain) in the tendon intact group (3/19 versus 6/18; RR 0.47, 95% CI 0.14 to 1.62; see Analysis 14.3). Both participants with moderate pain went on to have a mini-open biceps tenodesis at 18 and 28 months after diagnosis of an inflamed and scarred biceps tendon. There was no difference between the two groups in active shoulder elevation results at two years (see Analysis 14.4).

Continuing management (including rehabilitation) after surgical treatment

Wirbel 1999 tested the duration of immobilisation (one week versus three weeks) before starting physiotherapy after closed reduction and percutaneous fixation of displaced fractures in 77 patients. Wirbel 1999 reported that there were no statistically significant differences between the two trial groups in their functional results, assessed using the Neer score, at 3, 6 or at an average of 14.2 months. Data provided for unsatisfactory or worse outcome, as defined by the Neer score, at six months are consistent with this claim (see Analysis 15.1: 9/32 versus 10/32; RR 0.90, 95% CI 0.42 to 1.92; 64 participants). Premature removal of Kirschner wires because of loosening occurred in the five people in each group (see Analysis 15.2); these results, however, were not provided for the whole study population nor was it reported the treatment groups of five people who underwent open revision or hemiarthroplasty. Though similar numbers (three versus two) of people underwent removal of screws due to subacromial impingement after six months, the numbers of people in each group whose displaced tuberosity fractures were fixed with cannulated screws were not reported. Of the 21 participants followed up for more than two years, one developed partial necrosis of the humeral head but was symptom-free and had a full range of motion of his affected shoulder.

Agorastides 2007 reported the findings of early active-assisted mobilisation (after two weeks) versus late mobilisation (after six weeks) after cemented hemiarthroplasty in 49 of the 59 participants recruited in their trial. At one year follow-up, there were no significant differences between the two groups in function as rated by the Oxford shoulder score (see Analysis 16.1; MD -6.0, 95% CI -16.53 to 4.53; scale was 0 to 100) or the overall Con-

stant score (see Analysis 16.2). Two non-unions occurred in the early group but none of the differences in radiologically-assessed outcomes between the two groups was statistically significant (see Analysis 16.3). The differences between the two groups at one year in elevation and external rotation were neither statistically nor clinically significant (see Analysis 16.4).

ADDITIONAL SUMMARY OF FINDINGS *[Explanation]*

Early versus delayed mobilisation for non-surgically treated proximal humeral fractures

Patient or population: adults with minimally displaced or displaced (2-part or 3-part) proximal humeral fractures (4 trials)
Settings: various, including fracture clinics and physiotherapy
Intervention: early (within or at one week) mobilisation
Comparison: delayed (usual) mobilisation or physiotherapy after three or four weeks immobilisation

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	3 to 4 weeks immobilisation	Early mobilisation (≤ 1 week)				
Shoulder disability: Croft Shoulder Disability Score - Disability (1 or more problems) Follow-up: 1 year	**725 per 1000**[1]	**428 per 1000** (290 to 638)	**RR 0.59** (0.40 to 0.88)	82 participants (1 study)	⊕⊕◯◯ **low**[2]	Early mobilisation resulted in 297/1000 fewer people with one or more problems at 1 year (95% CI 87 fewer to 435 fewer)[3]
Number of treatment sessions (until independent function achieved) Follow-up: as described	The mean number of sessions was **14** in the usual timing group[4]	The mean number of sessions in the early group was **5.0 lower** (1.75 to 8.25 sessions lower)		86 participants (1 study)	⊕⊕◯◯ **low**[5]	This pertains to early recovery to a level that may vary with individual patients
SF-36 scores: pain & physical dimensions - all 3 dimensions 0-100: higher scores mean better quality of life) Follow-up: 16 weeks	The mean values for 3 dimensions in the delayed group[4] were: Physical functioning **69.2** Role limitation physical **39.7** Pain **59.9**	The mean values in the early group were: Physical functioning **0.70 higher** (9.91 lower to 11.31 higher) Role limitation physical **22.2 higher** (3.82 to 40.58 higher)		81 participants (1 study)	⊕⊕◯◯ **low**[6]	An overall score was not available. General physical functioning was high and comparable in the two groups. It is likely that the results for role limitation

		Pain **12.10 higher** (3.26 to 20.94 higher)				physical and pain are clinically important. This is consistent with the earlier recovery in independent function judged by treating physiotherapists (see above)
SF-36 scores: pain & physical dimensions - all 3 dimensions 0-100: higher scores mean better quality of life) Follow-up: 1 year	The mean values for 3 dimensions in the delayed group[4] were: Physical functioning **68.4** Role limitation physical **54.4** Pain **65.6**	The mean values in the early group were: Physical functioning **3.00 lower** (16.48 lower to 10.48 higher) Role limitation physical **5.60 higher** (13.75 lower to 24.95 higher) Pain **3.60 higher** (8.19 lower to 15.39 higher)		80 participants (1 study)	⊕⊕◯◯ **low**[6]	An overall score was not available. Results for all three dimensions are comparable in the two groups None of best estimates are likely to equate to clinically important differences
Quality of life assessment: EuroQol 5D (0: dead to 1: best health) Follow-up: 1 year	The mean EuroQol 5D score in the early group was **0.76**[4]	The mean EuroQol 5D score in the delayed group was 0.09 lower (0.21 lower to 0.03 higher)		39 participants (1 study)[7]	⊕◯◯◯ **very low**[8]	Similar results of little between-group differences of no clinical importance applied at 3 and 6 months
Adverse events: Shoulder complications Follow-up: 1 year	26 per 1000[9]	19 per 1000 (4 to 95)	**RR 0.73** (0.15 to 3.63)	259 participants (4 studies)	⊕◯◯◯ **very low**[10]	Reported shoulder complications were frozen shoulder (1 case), complex regional pain syndrome type 1 (2 cases) and treated subacromial impingement (2 cases) Early mobilisation resulted in 7/1000 fewer people with a shoulder complication at 1 year

						(95% CI 22 fewer to 69 more)
Adverse events: Fracture displacement and non-union Follow-up: 1 year	23 per 1000[9]	51 per 1000 (5 to 517)	**RR 2.20** (0.22 to 22.45)	106 participants (2 studies)	⊕◯◯◯ **very low**[10]	There were no cases of non-union. All three fracture displacements (none of which required surgery) occurred in one trial that included displaced fractures Early mobilisation resulted in 28/1000 more people with a fracture displacement at 1 year (95% CI 18 fewer to 494 more)

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

1. Control risk based on study data
2. Evidence downgraded one level for one level for imprecision (single small trial) and one level for indirectness (question over outcome measure's validity; the importance of individual problems will vary)
3. Two-year follow-up data from the same trial (74 participants) showed that based on a control risk of 595 per 1000 in the delayed group, early mobilisation resulted in 160/1000 fewer people with one or more problems at two years (95% CI 321 fewer to 90 more); very low quality evidence (see above footnote)
4. Data from control group of study
5. Evidence downgraded one level for imprecision (single small trial data) and one level for indirectness ('independent function' and physiotherapy discharge depicts an intermediate outcome)
6. Evidence downgraded one level for study limitations (several domains at unclear risk of bias) and one level for imprecision (single small trial data)

7. Evidence from a trial comparing 1 versus 4 weeks immobilisation for predominantly displaced fractures
8. Evidence downgraded one level for study limitations (study at high risk of bias) and two levels for imprecision (wide confidence intervals; single small trial data)
9. The assumed risk is the median control group risk across studies
10. Evidence downgraded one level for study limitations and two levels for imprecision (sparse data and wide confidence intervals)

DISCUSSION

Summary of main results

mThis review, which covers all non-pharmacological treatment and rehabilitation interventions for proximal humeral fractures in adults, now includes 31 trials involving a total of 1941 participants. The only multicentre trial recruited 250 participants (ProFHER 2015). With the increased availability of trials, we have been able to undertake further pooling of data compared with the last version, but this is still limited to four comparisons. We have undertaken substantive pooling in only one comparison, that of surgical versus non-surgical treatment, including patient-reported outcome measures of function and quality of life. This is presented first, below. The main results of the comparisons falling within the three other main treatment categories are then presented in turn. Where data allow, we have given the main results of individual comparisons in terms of the listed Primary outcomes.

Surgical treatment versus non-surgical treatment

Eight heterogeneous trials, with a total of 567 participants and 568 predominantly displaced fractures evaluated surgical intervention for displaced fractures, of which 73% (415) were three- or four-part fractures (Neer classification). Of note is that the majority of the fractures (146/250 = 58.4%) in ProFHER 2015 were either two-part (128) or one-part (18) fractures; the other seven two-part fractures were included in Kristiansen 1988. Table 1 summarises the main fracture types, the interventions and length of follow-up of the individual trials. Six trials specifically limited their trial populations to older people. Although ProFHER 2015 recruited adults of any age, the majority of trial participants were over 65 years (142/250 = 57%). Data for patient-reported functional scores and quality-of-life scores were available from the five more recent trials that are thus more likely to represent current practice. The main results of this comparison are presented in Summary of findings for the main comparison. The results apply to the majority of displaced proximal humeral fractures involving the surgical neck, but note should be taken of clear exceptions, such as where surgery is required for severe soft-tissue compromise, as well as the exclusion of fracture-dislocations, in ProFHER 2015. There was high quality evidence of no clinically important difference in patient-reported shoulder and upper-limb function at one- or two-year follow-up between surgical (primarily locking plate fixation or hemiarthroplasty) and non-surgical treatment (sling 'immobilisation') for the majority of displaced proximal humeral fractures. There was moderate quality evidence of no clinically important difference between the two groups in quality of life at two years. While this observation applied to interim follow-ups at six and 12 months, pooled data from four studies at six months showed a statistically significant effect. There was moderate quality evidence of little difference between the groups in mortality: although there were slightly more deaths in the surgery group, the 95% confidence interval also included the potential for a higher mortality after non-surgical treatment. Also of note is that, where reported, only one death was explicitly linked with treatment (surgery). There was moderate quality evidence of a higher risk of additional surgery in the surgery group: based on an illustrative risk of 40 subsequent operations per 1000 non-surgically treated patients, this amounts to an extra 43 subsequent operations per 1000 surgically treated patients (95% CI 7 to 104 more). There was also moderate quality evidence of a higher overall risk of adverse events after surgery; however, the 95% confidence intervals for adverse events also included the potential for a greater risk of adverse events after non-surgical treatment.

Methods of non-surgical management (including rehabilitation)

Non-surgical management, generally involving a period of arm immobilisation followed by physiotherapy, of (mainly) minimally displaced fractures is the focus of nine trials. Exceptionally, Torrens 2012 included a higher percentage of displaced fractures (81% = 34/42 fractures). There was a general recognition of the impaired function and serious complications, such as complex regional pain syndromes, that could follow a proximal humeral fracture.

Initial treatment, including immobilisation

When considering the extent and duration of initial immobilisation after a fracture, a balance is needed between the advantages of pain relief and avoidance of fracture displacement, and the consequences of immobilisation, notably joint stiffness and muscle atrophy.

Early versus delayed mobilisation

Of the four heterogeneous trials comparing early versus delayed mobilisation for minimally displaced or displaced fractures (Hodgson 2003; Kristiansen 1989; Lefevre-Colau 2007; Torrens 2012), only limited data, mainly for secondary outcomes, could be pooled from Lefevre-Colau 2007 and Torrens 2012.
Summary of findings 2 summarises the data relating to primary outcome measures for early versus delayed mobilisation in non-surgically treated fractures. With the exception of adverse event data provided by all four trials, most of these data are from Hodgson 2003. There was low quality evidence in favour of early mobilisation in terms of fewer people with shoulder problems at one year, of the need for fewer sessions of physiotherapy to achieve independent function, and of a better quality of life at 16 weeks in terms of less pain and less limitation of physical function. There was low quality evidence of no difference between early and delayed mobilisation in physical and pain aspects of quality of life at one year. There was very low quality evidence of no clinically important between-group differences in quality-of-life scores for people with mainly displaced fractures. There was very low quality

evidence of little difference between the two groups in shoulder complications and fracture displacement and non-union; the incidences of individual complications were low.

Type of bandage

The one quasi-randomised trial (28 participants with mainly minimally displaced fractures) provided very low quality evidence on the relative effects of two types of bandages, the Gilchrist arm sling versus the Desault body bandage (Rommens 1993). There was no report of PROMS nor data to support the claims of no between-group differences in functional outcome or fracture healing. More participants found the arm sling comfortable and acceptable compared with the body bandage.

Continuing management (rehabilitation) after initial treatment involving sling immobilisation

Instructions for home exercises versus physiotherapy

Two small trials including a total of 62 participants with minimally displaced fractures compared home exercises after receiving instructions versus supervised physiotherapy (Bertoft 1984; Lundberg 1979). Neither trial reported on PROMS for function or quality of life. There was very low quality evidence from single trials of little difference between the two groups in pain, change of therapy, adverse events, and range of motion.

Supervised exercises in a swimming pool plus home exercises versus home exercises alone

The trial making this comparison in 48 participants with minimally displaced fractures did not provide evidence that could be presented or tested in the analyses (Revay 1992). Revay 1992 claimed that the self-treatment group had better activities of daily living and joint mobility in the first two to three months but that the two groups had similar results at one year. Revay 1992 suggested that the supervised group had neglected their home exercises, which effectively undermines the aim of this trial.

Pulsed electromagnetic high frequency energy (PHFE)

Livesley 1992 hypothesised that pain was associated with contracture of the capsule of the glenohumeral joint and that PHFE would reduce inflammation and swelling, improving the end functional result. However, the trial (48 participants with minimally displaced fractures) failed to provide any quantitative data to support or refute this hypothesis.

Different methods of surgical management

Comparisons of different categories of surgical intervention

Five trials compared different methods of surgical management (Cai 2012; Hoellen 1997; Sebastiá-Forcada 2014; Smejkal 2011; Zhu 2011).

Open reduction with internal fixation using a locking plate versus a locking nail

There is very low quality evidence from one trial (Zhu 2011: 57 participants with two-part surgical neck fractures) of marginally better function (higher American Shoulder and Elbow Surgeon's scores) and slightly less pain after locking plate fixation compared with locking nail fixation at one year but not at three years. There was very low quality evidence of a higher rate of complications, including re-operation for screw penetration into the humeral head after plate fixation.

Open reduction with internal fixation using a locking plate versus minimally invasive fixation with distally inserted intramedullary K-wires

There is very low quality evidence from one trial (Smejkal 2011: 61 participants with two- or three-part fractures) of no difference between these two interventions for numbers of participants incurring a complication or in the Constant scores at two years follow-up.

Hemiarthroplasty versus internal fixation

With minimal opportunity for pooling, data from two small heterogeneous trials testing this comparison were presented separately.

Hemiarthroplasty versus open reduction and locking plate fixation

The very low quality evidence from one trial (Cai 2012: 32 participants with four-part fractures) of lower DASH scores (better function) and slightly higher EQ-5D scores (better quality of life) at one and two years may not equate to clinically important differences in either of these outcomes between hemiarthroplasty and locking plate fixation. Three participants in each group had a re-operation.

Hemiarthroplasty versus tension band wiring

There is very low quality evidence from one trial (Hoellen 1997: 30 participants with four-part fractures) of no differences between the two groups in the Constant scores or pain (18 participants). At one-year follow-up, all five reoperations occurred in the fixation group.

Reverse shoulder arthroplasty versus hemiarthroplasty

There is low quality evidence from one trial (Sebastiá-Forcada 2014: 62 participants with either three- or four-part fractures) of better patient-rated (Quick DASH) and composite shoulder function scores (UCLA and Constant scores) at a minimum of two years follow-up in the reverse shoulder arthroplasty (RSA) group. Although a condition-specific minimal clinically important difference is not available for QuickDASH, it is likely that the difference would have been clinically important to some extent. The clinically important differences favouring RSA in the Constant and UCLA scores will in part reflect the greater range of motion in the RSA group. Fewer people in the reverse arthroplasty group had a re-operation (one versus six) or had a complication (two versus 10).

Comparisons of different methods of performing an intervention in the same category

Seven trials compared different types or methods in the same intervention category (e.g. plating) (Buecking 2014; Fialka 2008; Lopiz 2014; Ockert 2010; Soliman 2013; Voigt 2011; Zhang 2011).

Deltoid-split approach versus deltopectoral approach for non-contact bridging plate fixation

There is very low quality evidence from one trial (Buecking 2014: 120 participants with two-, three- or four-part fractures) of no differences between groups in activities in daily living, re-operations or complications, Constant scores or pain at one year.

Polyaxial versus monoaxial locking plate fixation

Although two trials (Ockert 2010 and Voigt 2011: 180 participants with two-, three- or four-part fractures) made this comparison, most of the data were from Voigt 2011 (48 participants for function) and only data for re-operation were pooled. There was very low quality evidence of no between-group differences in function (DASH and simple shoulder test scores), re-operations and complications.

Locking plate: use of medial locking screws

There is very low quality evidence from one trial (Zhang 2011: 68 participants with two-, three- or four-part fractures) of medial locking screws resulting in fewer early losses of fixation and re-operations. However, the 95% CI results also included a higher risk of re-operations in the medial locking screws group. Based on the control risk of 154 re-operations per 1000 participants, medial locking screws resulted in 120 fewer re-operations (95% CI 149 fewer to 117 more). Although the medial screw group had statistically significantly higher Constant scores at 31-month follow-up, only part of the 95% CI included the minimal clinically important difference.

Nails: comparison of two types

There is low quality evidence from one trial (Lopiz 2014: 54 participants with two- or three-part fractures) of fewer adverse events, including re-operations and impingement, for the MPHN nail compared with the Polarus nail. Based on the control (Polarus nail) group risk of 423 re-operations per 1000 participants, the MPHN resulted in 308 fewer re-operations (95% CI 55 to 385 fewer). Of note is the very low quality evidence, as half as many participants in the MPHN group had rotator cuff symptoms. The MPHN group had higher Constant scores (very low quality evidence), which the authors linked with the lower incidence of rotator cuff symptoms in this group.

Hemiarthroplasty: comparison of two types

There was very low quality evidence from one trial (Fialka 2008: 35 out of 40 people with four-part fractures) for better function (Constant scores and range of motion) at one year for the EPOCA prosthesis when compared with the HAS prosthesis. Two participants in each group had a serious complication or pain requiring further treatment.

Hemiarthroplasty: tenodesis of the long head of the biceps (LHB) versus LHB tendon left intact

There was very low quality evidence from one trial (Soliman 2013: 45 people with four-part fractures undergoing hemiarthroplasty) of no between-group differences in complications at three months follow-up, in function (Constant score), in numbers of participants with shoulder pain or range of motion.

Continuing management (including rehabilitation) after surgical intervention

The need for and duration of immobilisation before commencing physiotherapy after surgery for displaced fractures was tested in two small heterogeneous trials for fixation and hemiarthroplasty respectively. There was very low quality and incomplete evidence from one trial (Wirbel 1999: 64 participants (of the 77 recruited)) of no difference between one week versus three weeks immobilisation after percutaneous fixation in the numbers of participants with an unsatisfactory or worse outcome based on the Neer outcome score at six months or incurring premature removal of K-wires failure (five in each group). There was very low quality evidence from one trial (Agorastides 2007: 49 participants (of the 59 recruited)) of no difference between participants mobilised after two weeks (which was current practice) after hemiarthroplasty versus those mobilised after six weeks in function (Oxford shoulder score or Constant score), radiological outcomes and range of motion at one year.

Overall completeness and applicability of evidence

To inform consideration of applicability of the evidence from individual trials, we give quite extensive details in the Characteristics of included studies on the study populations and interventions. Additionally, Table 2 shows our assessments for each trial of four aspects of relevance to ascertaining external validity: definition of the study population, description of the interventions, definition of primary outcome measures and length of follow-up. Clearly unhelpful is where there are incomplete descriptions of study inclusion (10 trials) and interventions (five trials). Five trials had less than one year's follow-up: Lefevre-Colau 2007 (six months), Livesley 1992 (six months), Ockert 2010 (six months) and Rommens 1993 (until fracture consolidation - time unspecified). Additionally, the minimum follow-up was six months in Lopiz 2014. Despite the claims of longer follow-up, the results seemed to apply to six months at most in Stableforth 1984. In Wirbel 1999, though follow-up of 21 participants was more than two years, the main results applied to the set follow-up at six months. Our setting of our criterion to one-year follow-up as acceptable is arbitrary and mainly reflects a reasonable timing for assessment of function. However, it should be noted that in terms of a full outcome assessment, data at one-year follow-up must be considered preliminary results only given that complications such as avascular necrosis and device failure may not become evident until later and functional recovery can still be ongoing.

The measurement of outcome was variable, though generally comprehensive. In most of the older trials, there was frequent use of non-validated or, at best, partly validated scoring systems such as the Neer (Neer 1970) and Constant (Constant 1987) systems, but also of simple rating systems for individual outcomes. Validated schemes such as the Oxford Shoulder Score (Dawson 1996) and Shoulder Rating Questionnaire (L'Insalata 1997) for subjective assessment of symptoms and function were not available at the time for the trials in earlier versions of this review. Nonetheless, some consideration of interobserver reproducibility and other aspects of validity was evident in the establishment of the Constant score in two trials (Lundberg 1979; Zyto 1997). Non-validated outcome assessment schemes, often with arbitrary criteria for grading overall outcome (excellent, good, fair, poor), are probably best viewed as 'blunt' and flawed instruments. This needs to be noted when viewing the results of many of the older included trials; in particular Kristiansen 1989, whose outcome assessment is almost completely based on the Neer scoring system. As noted also in our 2012 update, more recent trials continue to be better in this respect. Four of the eight newly included trials reported on PROMS for function: for example, Boons 2012 reported on the Simple Shoulder test; Cai 2012 on DASH; ProFHER 2015, the Oxford Shoulder Score; and Sebastiá-Forcada 2014, the QuickDASH. The continued use of the Constant score is notable, being reported by the newly included trials with the exception of ProFHER 2015, which did not conduct additional clinical examinations for the collection of such data.

The majority of the trials used Neer's fracture classification (Neer 1970). Problems, such as poor interobserver reproducibility and intraobserver reliability, with the classification of fractures according to the Neer and AO systems have been shown for both radiographs and computerised tomographic scans (Bernstein 1996; Brorson 2008; Sidor 1993; Siebenrock 1993; Sjoden 1997). This variation in the classification of fractures and hence diagnosis needs to be considered when interpreting the results of trials, both in respect to the comparability and composition of the intervention groups and in the applicability of the trial's findings. The limitations of the Neer classification scheme were also demonstrated by the identification of the valgus impacted four-part fracture as a separate category with a lower risk of avascular necrosis (Jakob 1991). Ideally a fracture classification system should act as a guide to treatment as well to enable the comparison of results from studies of patients with similar fracture patterns. However, other factors, such as osteoporotic bone, associated soft tissue injury and the patient's overall health and motivation, will also influence treatment choices and outcome. A recent study (Brorson 2012) looking at the agreement of surgeons' treatment recommendations in conjunction with the Neer classification concluded that the low observer agreement on the Neer classification may have less clinical importance than previously assumed. However, it noted that interobserver agreement on treatment did not exceed moderate levels. The purposefully pragmatic inclusion criteria used in ProFHER 2015 is noteworthy in this regard. These stipulated that the degree of displacement had to be sufficient for the treating surgeon to consider surgical intervention but did not have to meet the displacement criteria of Neer for inclusion in the trial. Post-recruitment classification by two independent surgeons of the baseline X-rays, resulted in the identification of 18 one-part fractures (see Table 1). Nonetheless these exceptions were judged sufficiently displaced that they would have been considered for surgical intervention in practice; where the exact observation of Neer's arbitrary criteria is rare.

While it is possible that all 31 trials are relevant to current practice somewhere in the world, it is likely that some interventions are now rarely used. These include body bandages as tested in Rommens 1993. Nowadays it is much more common practice to use either a 'collar and cuff' sling or a 'poly-sling' (these incorporate a chest strap that can be passed around the body). Additionally, the applicability of the findings from older trials, such as Stableforth 1984, is potentially less given subsequent changes in practice including the availability of new implants. These include locking plates, which are being increasingly used and promoted for these fractures (Thanasas 2009). Previously, we noted that the increasing use of locking plates for these fractures was reflected in the use of locking plates in more recently included trials (Handoll 2012). Another more recent development has been the use of reverse shoulder arthroplasty (RSA), typically for more complex four-part fractures in older people. This was tested in a

newly included trial (Sebastiá-Forcada 2014), with evidence pending from three ongoing trials comparing RSA with hemiarthroplasty (NTR3208; NCT02075476; SHeRPA), one ongoing trial comparing RSA with plating (DELPHI) and one ongoing trial comparing two types of RSA (NCT01086202).

Comments on individual comparisons

Surgical treatment versus non-surgical treatment

In our previous commentary for this comparison we noted that "Trials comparing surgical versus non-surgical interventions, or indeed different surgical interventions, risk losing currency as different implants and methods become available and fashionable." (Handoll 2012). We also noted the impact of surgical decision-making in favour of locking plating systems, which allow for stronger constructs and fixation of more complex fracture patterns in osteopenic bone with the potential for less soft-tissue stripping and compromise to the blood supply (Thanasas 2009). More recently for more complex (predominantly four-part) fractures, reverse shoulder arthroplasty is being promoted, as illustrated by its increasing use, for instance in the USA (Han 2015; Schairer 2015). These illustrate how evolving technology (and marketing forces) mitigates against applying the findings of these types of trials. However, more emphasis can be given to the evidence from the five more recent trials (Boons 2012; Fjalestad 2010; Olerud 2011a; Olerud 2011b; ProFHER 2015), all of which report patient-reported outcome measures of function and quality of life. When considering the validity and applicability of surgical trials, account needs to be taken also of fundamental variations in surgical practice, including facilities and operator expertise. In particular, operator expertise and the linked issue of the surgical learning curve, play a pivotal role in the validity and applicability of surgical trial findings. Awareness of these issues was behind the pragmatic decision in ProFHER 2015 for surgeons to use methods with which they are familiar rather than stipulate the type of surgery. Indeed, the pragmatic multicentre design of ProFHER 2015, including the constant emphasis on good standard practice and surgery by experienced surgeons (predominantly consultants), means that its results have immediate applicability at least in the setting where it was conducted (UK NHS trauma hospitals) and most likely in many other countries with similar surgical practice. Because of the dominance of the evidence from ProFHER 2015, particular note should be taken of its exclusion criteria (such as of fracture dislocations and two-part greater tuberosity fractures and other patterns not involving the surgical neck) and its study population, the composition of which shows the treatment uncertainty covered by this trial applied to the majority of displaced fractures of the proximal humerus. Additionally the lack of subgroup differences in ProFHER 2015, either for age (threshold of 65 years) or fracture type (tuberosity involvement or not; or Neer one- or two-part versus three- or four-part) strengthens the case for not differentiating treatment (use of surgery) on the basis of these characteristics. Nonetheless, in this trial and the other seven trials, six of which purposefully excluded younger adults, the evidence is predominantly from older people. This reflects the population distribution for these fractures (Karl 2015) but also the population for which the main treatment uncertainty applies.

Initial treatment, including immobilisation

Most of the evidence for the comparison of early versus delayed mobilisation came from Hodgson 2003 and thus applies primarily to the less severe fractures (minimally displaced two-part fractures). A survey sent to senior hospital physiotherapists working directly with orthopaedic patients revealed large variation in rehabilitation, in particular with regards to routine immobilisation, duration of immobilisation and timing of first contact with a physiotherapist, within and between hospitals in the UK (Hodgson 2003a; Hodgson 2006). A survey sent to the participating centres of ProFHER 2015, which included displaced fractures, found the recommended duration of arm immobilisation for non-surgically treated patients ranged from two to six weeks, with 29 (91%) of 32 UK hospitals recommending immobilisation of $\geq$ 3 weeks (Handoll 2015). This variation also needs to be viewed in the context of the type of arm immobilisation used, as methods such as collar and cuff provide support rather than rigid immobilisation. As noted by McKee 2007 in his commentary on Lefevre-Colau 2007, the applicability of this trial is limited by the intensive physiotherapy regimen used in both groups. Both practically and financially the 32 two-hour sessions of physiotherapy may be difficult for patients and health providers; notably, 10 participants withdrew from the trial because of difficulties in attending. In contrast, the mean numbers of treatment sessions in Hodgson 2003 were nine and 14 respectively in the two groups.

As stated above the body bandages tested in Rommens 1993, which compared the Gilchrist arm sling with the Desault body bandage, is rarely used in practice. The above-mentioned survey of practice carried out as part of ProFHER 2015 confirms this in the UK, where 'collar and cuff' slings, poly-slings and more rarely broad-arm slings are used (Handoll 2010).

Continuing management (rehabilitation) after initial treatment involving sling immobilisation

The three trials in this category that examined supervised versus home exercises were based in Sweden and possible differences in conventional physiotherapy regimens within and between countries, then and now, need to be taken into account when considering the application of trial findings. If they work, self-instruction and home-based exercise programmes are attractive for patients and conserve health care resources. There is some evidence from a Cochrane Review on fall prevention that older people, if well instructed and with intensive support (regular phone calls etc), can maintain a home-based exercise programme (Gillespie 2003;

Gillespie 2009). However, there will still be some patients with insufficient understanding or motivation to perform the required exercises.

Different methods of surgical management

Most of the recent research activity, in both published and registered trials, evaluates different types of surgery. We now distinguish between trials comparing different categories of surgical interventions (tested by five trials) and trials comparing different methods of performing an intervention in the same category (tested by seven trials).

Comparisons of different categories of surgical intervention

The variety of available implants in the same category can limit the applicability and usefulness of trials comparing different categories of surgical intervention by comparisons of specific implants. Nonetheless, the comparison by Zhu 2011 of one of two locking plates versus a locking nail is very pertinent in terms of providing a useful investigation of the appropriateness of the current trend from locking nails to plates. This trial is too small to establish the superiority of one method over the other but it does provide some evidence of better function in the plate group at one year, and possibly for longer, although at a potentially greater risk of surgical complications and initially more invasive surgery. The comparison by Smejkal 2011 of a locking plate versus minimally invasive fixation with distally inserted multiple intramedullary K-wires (the Zifko method of minimally invasive fixation) is of relevance to current practice but, while data from Smejkal 2011 lend support to the use of the Zifko method in terms of it being a less extensive surgical procedure with potentially an earlier recovery than plate fixation, there were inadequate data on longer term function and outcome.

Again, the trial comparing hemiarthroplasty versus open reduction and locking plate fixation was too small to inform practice (Cai 2012). The absence of intraoperative conversions for the open reduction and internal fixation (ORIF) group to hemiarthroplasty or early failures is notable for a series of 13 displaced four-part fractures and fracture-dislocations and may indicate differences in assessing and dealing with problematic or failed fixation in this centre compared with other centres. Hoellen 1997, a flawed trial with only one-year follow-up, considered only one of several shoulder prostheses now available (the prosthesis was cemented in place) in their comparison with tension band wiring.

The comparison of reverse shoulder arthroplasty (RSA) versus hemiarthroplasty tested in Sebastiá-Forcada 2014 is very topical, as shown also by the three ongoing trials that are making the same comparison (NCT02075476; NTR3208; SHeRPA). The prostheses compared within each of these four trials come from only one manufacturer. However, the three ongoing trials examines prosthesis from three different manufacturers. Prostheses made by different manufacturers will differ to some extent; however, the variation between prostheses from different manufacturers is likely to be of lesser importance clinically than the large differences between RSA and hemiarthroplasty. In terms of applicability, Sebastiá-Forcada 2014 is mainly limited by being a single-centre trial with the participants being operated on by two surgeons.

Comparisons of different methods of performing an intervention in the same category

The trial (Buecking 2014) comparing two approaches (deltoid-split approach versus deltopectoral) for non-contact bridging plate fixation had two notable limitations in terms of external validity. One was the absence of criteria for excluding patients for whom hemiarthroplasty was planned. The second was the inappropriate interpretation of the Lawson quality-of-life score. The two trials (Ockert 2010; Voigt 2011) comparing 'polyaxial' (where surgeons had greater control in their positioning of screws into the bone) versus 'monoaxial' locking plate fixation found no difference between the two methods. With no report of functional outcome, Ockert 2010 contributed relatively little to this question. Voigt 2011, which was a stronger trial but still insufficient to be conclusive, pointed out that the "majority of surgeons chose the same screw directions for the polyaxial screws as already exist in the fixed angle plate". In their 2014 publication, Ockert 2010 also found that polyaxial screws were placed similarly to monoaxial screws. Of note also is the differences in the types of screws in the two implants in Voigt 2011, which could in some respects alter the question. Zhang 2011 tested the use of medial support locking screws for fixation using the PHILOS locking plate. While Zhang 2011 did not provide conclusive evidence of clinical benefit of the enhanced stabilisation of this commonly used plate, the direction of effect is consistent with the theoretical advantages for medial support screws.

In their comparison of the MultiLoc Proximal Humeral Nail (MPHN) versus the Polarus nail, Lopiz 2014 found the newer "straight" nail (the MPHN) resulted in fewer adverse events (screw loosening, impingement, rotator cuff symptoms) than the "curved" Polarus nail. This is plausible given the different design features of the MPHN that attempt to avoid the various problems, including impingement, that have been identified when using the Polarus nail. However, some consideration is also required of the rather high incidence of adverse events for the Polarus nail and the general inadequacies of tests for rotator cuff symptoms (Hanchard 2013).

Fialka 2008 compared two shoulder prostheses but although the authors ascribed the different functional outcomes to tuberosity fixation, other design differences may account for these results. These include a different stem finish and a more accurate recreation of pre-operative humeral geometry with the EPOCA prosthesis. The study population of Soliman 2013, which compared tenodesis of the long head of the biceps (LHB) versus LHB tendon left intact in people undergoing hemiarthroplasty, was exceptional in being younger (aged 45 to 60 years) than all other trial

populations in this review and younger than the population for whom hemiarthroplasty is more typically used. Although the inclusion criteria included more severe injuries such as head-splitting fractures, Soliman 2013 provided insufficient criteria on which to judge participant suitability for hemiarthroplasty. Additionally of note, is the absence of spontaneous ruptures of the long head of biceps.

Continuing management (including rehabilitation) after surgical intervention

The need for and duration of immobilisation before commencing physiotherapy after surgical treatment is likely to depend on the method of fixation or type of prosthesis; and also other factors such as bone quality. While neither trial (Agorastides 2007; Wirbel 1999) found conclusive evidence for early mobilisation, such as offering any functional advantage, it can also be observed that the evidence was inconclusive for later mobilisation too, such as avoiding destabilisation of the fracture fixation after percutaneous fixation or tuberosity fixation after hemiarthroplasty.

Quality of the evidence

As noted in Handoll 2012 and continues to apply in this update, more recent trials generally have better study design (e.g. they have appropriate random sequence generation and allocation concealment, and thus are at low risk of selection bias) and reporting (e.g. including participant flow diagrams). Nonetheless, as shown by Figure 2, many of the included trials had serious shortcomings and are at high risk of bias that could affect the validity of their findings. The main but generally unavoidable shortcoming in trials testing physical and surgical interventions was the lack of blinding, which is unavoidable to a great degree. Twenty-one trials were considered at high risk of outcome assessment bias for function and other subjective outcomes. The risk of bias resulting from a high loss to follow-up or exclusion of participants from the analyses was considered high in 13 trials, two of which were new to this version (Buecking 2014; Soliman 2013). Most comparisons were carried out in small single trials only; there is clearly a need for caution in interpreting the results of small trials which demonstrate 'no evidence of an effect' rather than 'evidence of no effect'. Insufficiencies in quantity and quality of the evidence still preclude the drawing of robust conclusions for most of the comparisons evaluated by the included trials.

Only one of the eight newly included trials had prospective trial registration and a published protocol (ProFHER 2015). While this is discouraging at present, it is notable that the increased research activity in this previously overlooked area is also associated with far more prospective trial registration as well as publication of trial protocols. Both these items show the greater use of robust methodology that is required to minimise bias. Additionally, there is a growing interest in multicentre trials. Seven of the 21 ongoing trials are multicentre.

The results of the GRADE assessment of the quality of evidence for the individual comparisons are summarised below. With the exception of the evidence for the comparison of surgical versus non-surgical treatment, most of the GRADE assessments for the other comparisons were low or very low quality. This typically reflects the insufficiency of the evidence from small single trials which have limitations in design, conduct, analysis and reporting, putting them at high risk of bias.

Surgical treatment versus non-surgical treatment

- The quality of evidence assessments for difference outcomes for this comparison ranged from moderate to high (for details please see Summary of findings for the main comparison).

Initial treatment, including immobilisation

- **Early versus delayed mobilisation:** the quality of evidence assessments for difference outcomes for this comparison ranged from very low to low (for details please see Summary of findings 2).
- **Type of bandage (Gilchrist arm sling versus the Desault body bandage):** the quality of evidence assessments for all reported outcomes were very low. The evidence was downgraded two levels for serious study limitations reflecting a serious risk of bias (including selection bias: quasi-randomised trial) and one level for imprecision (single small trial: 28 participants).

Continuing management (rehabilitation) after initial treatment involving sling immobilisation

- **Instructions for home exercises versus physiotherapy:** the quality of evidence assessments for all reported outcomes were very low. The evidence was downgraded one level for study limitations reflecting a high risk of bias and two levels for imprecision (evidence from single small trials: 20 and 42 participants).
- **Supervised exercises in a swimming pool plus home exercises versus home exercises alone:** the quality of evidence assessments for all reported outcomes were very low. There is no quantitative evidence available for this comparison.
- **Pulsed electromagnetic high frequency energy (PHFE):** the quality of evidence assessments for all reported outcomes were very low. There is no quantitative evidence available for this comparison.

Different methods of surgical management

Comparisons of different categories of surgical intervention

- **Open reduction with internal fixation using a locking plate versus a locking nail:** the quality of evidence assessments for all reported outcomes were very low. The evidence was downgraded one level for study limitations reflecting a high risk of bias and two levels for imprecision (evidence from 57 participants in one trial).
- **Open reduction with internal fixation using a locking plate versus minimally invasive fixation with distally inserted intramedullary K-wires:** the quality of evidence assessments for all reported outcomes were very low. The evidence was downgraded two levels for study limitations reflecting a serious risk of bias and one level for imprecision (evidence from 55 participants in one trial).
- **Hemiarthroplasty versus open reduction and locking plate fixation:** the quality of evidence assessments for all reported outcomes were very low. The evidence was downgraded one level for study limitations reflecting a high risk of bias and two levels for imprecision (evidence from 32 participants in one trial).
- **Hemiarthroplasty versus tension band wiring:** the quality of evidence assessments for all reported outcomes were very low. The evidence was downgraded two levels for study limitations reflecting a serious risk of bias and one level for imprecision (evidence from 30 participants in one trial).
- **Reverse shoulder arthroplasty versus hemiarthroplasty:** the quality of evidence assessments for all reported outcomes were low. The evidence was downgraded one level for study limitations reflecting unclear risk of bias in several domains and one level for imprecision (evidence from 62 participants in one trial).

Comparisons of different methods of performing an intervention in the same category

- **Deltoid-split approach versus deltopectoral approach for non-contact bridging plate fixation:** the quality of evidence assessments for all reported outcomes were very low. The evidence was downgraded two levels for study limitations reflecting a serious risk of bias and one level for imprecision (wide confidence intervals; evidence from 120 participants in one trial). The evidence would have been further downgraded one level for indirectness because of the possible misapplication of the Lawson quality-of-life score.
- **Polyaxial versus monoaxial locking plate fixation:** the quality of evidence assessments for all reported outcomes were very low. The evidence was downgraded one level for study limitations reflecting a serious risk of bias and two levels for imprecision (wide confidence intervals; evidence for function from 48 participants in one trial).
- **Locking plate - use of medial locking screws:** the quality of evidence assessments for all reported outcomes were very low. The evidence was downgraded one level for study limitations reflecting unclear risk of bias in several domains and two levels for imprecision (wide confidence intervals; evidence from 68 participants in one trial).
- **Intramedullary nails: MPHN versus Polarus:** the quality of evidence assessments for the reported outcomes were low or very low. The evidence was downgraded one or two levels for study limitations reflecting the high risk of outcome assessment bias and the unclear risk of bias relating to detection given the large range in follow-up (6 to 22 months) for some outcomes, and one level for imprecision (wide confidence intervals; evidence from 54 participants in one trial).
- **Hemiarthroplasty - comparison of the EPOCA versus the HAS prosthesis:** the quality of evidence assessments for all reported outcomes were very low. The evidence was downgraded two levels for study limitations reflecting a serious risk of bias and one level for imprecision (inadequate data presented; evidence from 35 participants in one trial).
- **Hemiarthroplasty - tenodesis of the long head of the biceps (LHB) versus LHB tendon left intact:** the quality of evidence assessments for all reported outcomes were very low. The evidence was downgraded two levels for study limitations reflecting a serious risk of bias and one level for imprecision (evidence from 45 participants in one trial).

Continuing management (including rehabilitation) after surgical intervention

- **One week versus three weeks immobilisation after percutaneous fixation:** the quality of evidence assessments for all reported outcomes were very low. The evidence was downgraded two levels for study limitations reflecting a serious risk of bias and one level for imprecision (evidence at six months from 64 participants in one trial).
- **Mobilisation after two weeks versus six weeks following hemiarthroplasty:** the quality of evidence assessments for all reported outcomes were very low. The evidence was downgraded two levels for study limitations reflecting a serious risk of bias and one level for imprecision (evidence from 49 participants in one trial).

Potential biases in the review process

While our search was comprehensive it is likely that we have failed to identify some randomised trials, particularly those reported only in abstracts or in non-English language publications. We may also have overlooked mixed-population trials that included proximal humeral fractures as a subgroup. However, we are almost certain that we have not overlooked trials that would provide definitive evidence that could inform practice. It is clear, from the growing awareness and imperative of trial registration, that such trials are now in progress. We prepared the review using systematic processes throughout, including contacting trial investigators for clarification and missing data. We describe the dilemma presented

in the pooling of data from clearly heterogeneous trials for the surgical treatment versus non-surgical treatment comparison in the Effects of interventions. This is, however, compatible with the overall question and notably the pooled analyses did not result in statistically significant heterogeneity.

Agreements and disagreements with other studies or reviews

Several new systematic reviews, none of which cover all treatment options, were identified via the search update. The only rehabilitation review examined the effects of exercise in people with select upper limb fractures including proximal humeral fractures (Bruder 2011). Two reviews compared surgical versus non-surgical intervention (Li 2013; Mao 2014). Li 2013 limited surgery to internal fixation. One review compared arthroplasty versus 'joint preservation' that was either non-surgical treatment or internal fixation (Zhang 2014). Two compared arthroplasty versus internal fixation (Dai 2014; Gomberawalla 2013). Dai 2014 limited internal fixation to locking plate fixation. Two reviews compared reverse shoulder arthroplasty versus hemiarthroplasty (Mata-Fink 2013; Namdari 2013). All eight reviews, four of which included evidence from a broader spectrum of study designs (Dai 2014; Gomberawalla 2013; Mata-Fink 2013; Namdari 2013), reported the limitations in the available evidence. Unlike our review, with its later search date, none of the three reviews comparing surgical versus non-surgical treatment included ProFHER 2015 and neither of the two reviews comparing RSA with hemiarthroplasty included the first randomised trial on this topic (Sebastiá-Forcada 2014).

AUTHORS' CONCLUSIONS

Implications for practice

There is high or moderate quality evidence that, compared with non-surgical treatment, surgery does not result in a better outcome at one and two years after injury for people with displaced proximal humeral fractures involving the humeral neck and is likely to result in a greater need for subsequent surgery. The evidence does not cover the treatment of two-part tuberosity fractures, fractures in young people, high energy trauma, nor the less common fractures such as fracture dislocations and head splitting fractures.

There is insufficient evidence from randomised controlled trials to inform the choices between different non-surgical interventions, different surgical interventions, or different rehabilitation interventions for these fractures.

Implications for research

The availability of high quality evidence primarily from a sufficiently powered multicentre randomised trial (ProFHER 2015) is the key reason why this review can now inform on the use of surgery for the majority of displaced fractures. There is a need for similar trials to help address other key treatment uncertainties. Decisions on priority topics should consider the coverage of the current evidence base as well as the topics covered by the ongoing trials. Of particular note is that three ongoing trials are already comparing reverse shoulder arthoplasty versus hemiarthoplasty.

Although the identification of priority topics requires input from others, including patients, we suggest that research should be focused primarily on optimising non-surgical treatment. Where randomised trials are warranted, these should use standard and validated outcome measures, including patient-reported measures of functional outcome and quality of life, and also assess resource implications. They should also meet the CONSORT criteria for design and reporting of non-pharmacological studies (Boutron 2008) and subsequent developments including the adequate reporting of interventions (Hoffmann 2014).

This Cochrane review should be maintained and updated as further randomised controlled trials become available. The authors would be pleased to receive information about any other randomised controlled trials relating to the treatment of these fractures.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Agorastides 2007

Methods	Randomised using sequentially numbered sealed envelopes Assessor blinding: stated for Constant Shoulder Assessment and Oxford scores at 6 and 12 months Loss to follow-up at 1 year: 10 (all exclusions: 4 wrong prosthesis; 1 pathological fracture; 1 deep infection requiring further procedure; 2 initial greater tuberosity malpositioning; 2 did not attend follow-up visits)
Participants	Royal Liverpool Hospital, Liverpool, UK Period of study recruitment: October 2002 to October 2003 59 patients with displaced proximal humeral fractures, 3-part or 4-part or articular fractures who were treated with cemented hemiarthroplasty. Isolated non-pathologic fractures < 6 weeks old. Physiologically old patients with poor bone quality. Informed consent. Exclusion criteria: no extra information Of 49: 39 female, 10 male; mean age 70 years, range 34 to 85 years
Interventions	Intervention started post surgery (mean 10 days; range 1 to 30 days after injury) 1. Early active-assisted mobilisation (after 2 weeks). Arm kept in sling in neutral rotation for 2 weeks; only pendulum and elbow exercises allowed. Between weeks 3 and 6, progressed to active-assisted exercises; from week 7, to active exercises. 2. Late mobilisation (after 6 weeks). Arm kept in sling in neutral rotation for 6 weeks; only elbow exercises allowed. From week 7 to week 12, progressed from pendulum to active-assisted exercises; from week 13, to active exercises Both mobilisation protocols were supervised by a team of specialist shoulder physiotherapists
Outcomes	Length of follow-up: 1 year; also assessed at 2 and 6 weeks, and 3 and 6 months (coinciding with outpatient visits) Oxford shoulder score Constant shoulder score (mobility, strength, pain, activities of daily living) Range of motion: elevation, external and internal rotation Complications Radiological assessment: greater tuberosity migration; superior luxation of prosthesis
Notes	The early mobilisation regimen represented normal practice at the hospital

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method: "Patients were randomly allocated"

Allocation concealment (selection bias)	Unclear risk	"Randomization took place in the operating theater after the procedure, by use of sequentially numbered, sealed envelopes."
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	"At the 6- and 12-month visits, an independent blinded observer completed the Constant Shoulder Assessment and Oxford scores." However, care providers and participants were not blind to allocation and assessment of complications was not blinded either
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	No accounting of these, but lack of blinding unlikely to affect reporting of these
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	High risk	Incomplete account of participant flow, with exclusion of 10 participants from the analyses
Incomplete outcome data (attrition bias) Death, reoperation	High risk	No accounting of these outcomes, but incomplete account of participant flow, with exclusion of 10 participants from the analyses
Selective reporting (reporting bias)	High risk	No protocol available. May have been stopped early, greater tuberosity migration not specifically listed in brief trial entry in the National Research Register (UK)
Balance in baseline characteristics?	Unclear risk	Incomplete data to back up claims of lack of baseline differences as these given only for 49 (10 excluded) but a 5-year difference in mean age (72 versus 67 years)
Free from performance bias?	Unclear risk	Although 3 upper limb surgeons performing the operations agreed to the same procedures a different uncemented prosthesis was used in 4 subsequently excluded participants. "Both mobilization protocols were supervised by a team of specialist shoulder physiotherapists."

Bertoft 1984

Methods	Use of permutation table, single-blind, independently administered Assessor blinded Loss to follow-up at 1 year: 7/20 (2 excluded)
Participants	Central hospital, Vasteras, Sweden Period of study recruitment: not stated 20 patients with non or minimally displaced proximal humeral fractures (7 had fracture of the greater tubercle); sling for 10 days. Exclusion criteria: no information 17 female, 3 male; mean age 64 years, range 50 to 75 years
Interventions	Interventions started 10 to 12 days post injury, after removal of sling. 1. Instructed self-exercise: patients instructed to train 5 to 10 minutes, 4 to 5 times daily. They had three training sessions (day 1, weeks 3 & 8 post injury) 2. Conventional physiotherapy: 9 sessions (average 20 to 30 minutes), 1 to 2 times each week, over 10 to 12 weeks. No thermoelectrotherapy. Assigned: 10/10 Completed (> 1 year): 7/6
Outcomes	Length of follow-up: 1 year; also assessed at 3, 8, 16 & 24 weeks Range of motion: forward flexion (graph), abduction, internal & external rotation Functional movements: placing hand on neck, placing hand on back Pain: when placing hand on neck: combing hair (graph) Isometric muscle strength: vertical & horizontal pushing Change of treatment requested
Notes	The 2 excluded participants were in the control group: 1 died and 1 underwent an operation

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Mention of "permutation table" and "randomized controlled" trial
Allocation concealment (selection bias)	Low risk	"A third person was responsible for the randomization procedure and kept the key to the permutation table"
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	"A second physiotherapist examined the patients. She did not know to which group the patient belonged, and the patients were instructed not to tell her." However, there is no guarantee of blinding and, for practical reasons, neither participants nor care provider were blinded

Bertoft 1984 (*Continued*)

Blinding (performance bias and detection bias) Death, reoperation	Low risk	Lack of blinding unlikely to affect assessment of these outcomes
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	Participant flow provided but large loss to follow-up (7/20 = 35%)
Incomplete outcome data (attrition bias) Death, reoperation	Low risk	Participant flow provided
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge this.
Balance in baseline characteristics?	Unclear risk	Incomplete data to back up claims of lack of baseline differences but a 4-year difference in mean age between groups (66 versus 62 years)
Free from performance bias?	Low risk	No indication of performance bias.

Boons 2012

Methods	Method of randomisation: computer-generated randomisation sequence; sealed opaque envelopes stored in statistician's room Assessor blinding: not blinded Loss to follow-up at 12 months: 3/50 (2 withdrawn; 1 died)
Participants	Rijnstate Hospital, Arnhem, The Netherlands Period of study recruitment: June 2004 to July 2009 50 patients with an acute displaced (based on Neer's criteria) 4-part proximal humeral fractures (8, 4 in each group, had valgus impacted fractures; no mention of fracture-dislocations). Age 65 or older. Informed consent. Exclusion criteria: pre-existing mental disorders (dementia) or unable to provide informed consent or answer the questionnaires; disabling disorder or additional trauma to the affected arm; pathological or open fracture; associated neurovascular injury; pre-existing impairment of the contralateral shoulder; unable to understand Dutch; unable to participate in the rehabilitation protocol; contraindicated for surgery (American Society of Anesthesiologists [ASA] physical status 4) 47 female, 3 male; mean age 78 years, range not stated
Interventions	Randomisation was performed in the first week after fracture. 1. Surgery: operation within 7 days of injury. Under general anaesthesia. Humeral head replacement using a deltopectoral approach with the Global Fx shoulder fracture endoprosthesis (DePuy, Leeds, UK). All prostheses were cemented. Cancellous bone graft from the head fragment was applied on the proximal stem before restoration of the tuberosities. Nonabsorbable sutures used to encircle the tuberosities to "enhance anatomic restoration". (All patients had prophylactic antibiotics.) Post surgery: shoulder immobiliser for 6 weeks.

	2. Non-surgical treatment: shoulder immobiliser for 6 weeks. Rehabilitation was same in both groups: Experienced shoulder physical therapists instructed the patients for 40-minute sessions three times a week up to 12 weeks. Up to 2 weeks light passive ROM movements; between 2 and 6 weeks, passive ROM up to 45 degrees forward flexion and abduction and active ROM up to 30 degrees forward flexion and abduction were allowed if pain control adequate; no external rotation. After 6 weeks, unlimited passive glenohumeral exercise, with active ROM up to 90 degrees in forward flexion and abduction. External rotation was allowed up to 30 degrees. After the 3-month visit, patients were seen by the physical therapist every month until the 12-month follow-up, with an emphasis on maximizing ROM, strength and return to daily activities. Assigned: 25/25 Completed (at 1 year): 23/24 (based on text account)
Outcomes	Length of follow up: 1 year; also assessed at 1 & 6 weeks and 3 months Constant shoulder score (contralateral shoulder measured at 1 week follow-up as reference) SST (Simple Shoulder Test) Pain (VAS) Disability (VAS) Abduction strength (contralateral shoulder measured at 1 week follow-up as reference) Range of motion: abduction, flexion, external rotation, internal rotation (lumbar level) Complications: Non-union, osteonecrosis, pain and impingement, heterotopic ossification, infection, implant dislocation (head stem separation), secondary migration of greater tuberosity, secondary rotator cuff tear (from migration of hemiarthroplasty), non-union of greater tuberosity Subsequent surgery (reasons: head stem separation and pain and impingement)
Notes	Additional information on group of a withdrawn participant (had deteriorating condition) and SST scores (incorrect in Table 2 in article) requested from Dr van Loon (14 Feb 2015). Response from Dr Boons (12 March 2015) identified group of the withdrawn participant (hemiarthroplasty) and provided the raw data for STT

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"patients were randomly allocated to non-operative treatment or hemiarthroplasty. The randomization list was generated by an independent statistician". "A computer-generated variable block schedule was used. ."
Allocation concealment (selection bias)	Low risk	"the resulting treatment allocations were stored in sealed opaque envelopes in the statistician's room."

Boons 2012 (*Continued*)

Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	No mention of independent or blinded assessment. Initial care providers could not be blinded for these contrasting interventions
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Lack of blinding unlikely to affect assessment of these outcomes
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Low risk	Active and systematic surveillance. Low loss to follow-up (6%). Author's response resolved problem over contradictory statements in trial report on group allocation for one participant
Incomplete outcome data (attrition bias) Death, reoperation	Low risk	Active and systematic surveillance. Low loss to follow-up (6%). Author's response resolved problem over contradictory statements in trial report on group allocation for one participant
Selective reporting (reporting bias)	Unclear risk	No protocol. Outcome measures well described but the problems with the STT scores (incorrect data and direction of effect) gave slight cause for concern
Balance in baseline characteristics?	Low risk	No difference in baseline characteristics, including in numbers of valgus impacted (4 versus 4) fractures
Free from performance bias?	Low risk	Standard procedure performed by two experienced shoulder surgeons. Same rehabilitation protocols including during shoulder immobilisation

Buecking 2014

Methods	Method of randomisation: block randomisation stratified by type of fracture; pre-sealed randomisation envelope given by study staff to surgeon before surgery Assessor blinding: not blinded (independent observer) Loss to follow-up at 12 months: 13/120 (9 lost to follow-up; 4 died)
Participants	University hospital of Giessen and Marburg, Marburg, Germany Period of study recruitment: December 2009 to November 2011 120 patients with displaced proximal humeral fractures (Neer 2-part; and 3- or 4-part). Age 18 or older. Written consent. Exclusion criteria: glenohumeral dislocation, concomitant ipsilateral fractures of the arm or forearm, malignancy-related fractures, multiple trauma, other surgery planned

	(prosthesis or a longer plate) 92 female, 28 male; mean age 68 years, range 63 to 72
Interventions	Randomisation was performed prior to surgery; timing not stated All participants received a plate osteosynthesis with the non-contact bridging plate for the proximal humerus. In addition to the plate, a cable wire was used to fix the greater tuberosity in 3 and 4 part fractures. All patients received a single-shot antibiotic. 1. Deltoid-split approach: anterolateral 3 cm deltoid split with two small incisions for the three locking screws in the humeral shaft. 2. Deltopectoral approach: fracture was exposed through a classical anterior approach; a 10 to 12 cm incision was begun at the tip of the coracoid process and run medially in the direction of the deltoid muscle Rehabilitation after surgery was same in both groups. Operated shoulder immobilised for first 2 days; then passive and limited active motion started. For 3- and 4-part fractures, only limited assisted abduction up to 90º was allowed for first 6 weeks Assigned: 60/60 Completed (at 1 year): 48/42
Outcomes	Length of follow-up: 1 year; also assessed at 6 weeks and 6 months Constant shoulder score (normalised) Activities of daily living (Lawton 1969) Pain (VAS) Complications: humeral head necrosis (0), axillary nerve damage (0), deep infection, screw perforations, implant loosening at head or shaft, inadequate reduction, implant failure from subsequent fall Change during primary operation: primary prosthesis inserted Re-operations (for complications and at request of patient) Fluoroscopy use Length of surgery Hospital stay
Notes	The range of scores for Lawton's instrumental activities of daily living score is from 0 to 8 (best score); those reported in this trail report include mean scores of 11 up to 21. Since there is no explanation for this in the trial report, the meaning of the data is unclear and they are not presented in the review

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"With the use of a block randomization stratified by type of fracture (two-part fractures versus three- and four part fractures), patients were randomized to either the deltoid-split or the deltopectoral approach." Not quite enough detail to be certain; although likely

Buecking 2014 (*Continued*)

Allocation concealment (selection bias)	Low risk	"Presealed randomization envelopes were given by the study staff to the attending surgeon before surgery."
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	"Standardised follow-up examinations were performed at 6 weeks, 6 months, and 12 months after surgery by the same independent observer. .." However, the incision would still have been obvious
Blinding (performance bias and detection bias) Death, reoperation	High risk	Unclear if choices for primary or secondary surgery were influenced by prior knowledge. No revisions to hemiarthroplasty in the deltoid-split group could indicate that reoperation was only considered if a deltopectoral approach could be enlarged
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	High risk	Inappropriate post-randomisation exclusions: primary prosthesis (2 versus 4), secondary prosthesis (5 versus 2) and enlarged deltopectoral approach during revision surgery (0 versus 4)
Incomplete outcome data (attrition bias) Death, reoperation	Low risk	Inappropriate post-randomisation exclusions: primary prosthesis (2 versus 4), secondary prosthesis (5 versus 2) and enlarged deltopectoral approach during revision surgery (0 versus 4). However, these were known for these outcomes. Similar numbers were not reachable (4 versus 5)
Selective reporting (reporting bias)	Unclear risk	No protocol. Although systematic data collection and all outcomes reported, the disparity between the reported data for the Lawton instrumental activities of daily living score (maximum 8) and the actual scores presented in the text is of some concern
Balance in baseline characteristics?	Low risk	Good balance in baseline characteristics
Free from performance bias?	Low risk	Operations were performed by 3 senior surgeons who were trained in both techniques. Equivalent care programmes in both groups

Cai 2012

Methods	Method of randomisation: no details Assessor blinding: not blinded (independent observer) Loss to follow-up at 24 months: 5/32 (4 lost to follow-up; 1 died)
Participants	Shanghai Tenth People's Hospital of Tongji University, Shanghai, China Period of study recruitment: April 2005 to March 2010 32 patients with acute displaced 4-part proximal humeral fracture of the surgical neck (Neer classification). At least one tubercle needed to be displaced more than 10 mm in relation to the head fragment but the other did not need to meet this criterion (thus 3-part fractures were also acceptable); see Notes. Age 67 or older with low energy trauma. Independent living conditions (not institutionalised), and no severe cognitive dysfunction (3 or more correct answers on a 10-item Short Portable Mental Status Questionnaire [SPMSQ]) Exclusion criteria: completely displaced shaft in relation to the head fragment, such as a fracture without bony contact; valgus impacted fracture, previous shoulder problems 27 female, 5 male; mean age 72 years, range 67 to 86
Interventions	Randomisation was performed after clearance by an anaesthetist prior to surgery; timing not stated All patients received a single dose of antibiotic preoperatively. 1. Hemiarthroplasty using the DuPuy prosthesis with suturing of tuberosities. Cemented stem. Bone graft from removed humeral head used to restore the humeral offset 2. Open reduction and internal fixation with Philos plate. Suturing of tuberosities Postoperative arm sling for 4 weeks (optional thereafter). All patients referred to physiotherapy. Pendulum exercises and passive elevation/abduction up to 90° were started on postoperative day 1. After 4 weeks, the patients were allowed free active range of motion Assigned: 19/13 Completed (at 2 years): 15/12
Outcomes	Length of follow-up: 2 years; also assessed at 4 and 12 months DASH Constant shoulder score Pain (VAS) Complications (relating to re-operations): non-union, fixation failure, dislocation, infection, prosthesis loosening Re-operations (for complications) Length of surgery
Notes	One participant initially had a 3-part greater tuberosity fracture but at surgery, the lesser tuberosity was also found to be displaced > 1 cm. Hence all had 4-part fractures. Three of 32 participants had fracture dislocations Sent email to Dr Li requesting details of the randomisation method and clarification on deaths on 24 May 2015

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Cai 2012 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	"the patients were randomized". No other details.
Allocation concealment (selection bias)	Unclear risk	"the patients were randomized". No other details.
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	Not blinded even though there was some independent assessment at final follow-up: "Final 24-month follow-up was performed by an independent orthopedic surgeon (K. T.) not involved in treatment."
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Lack of blinding less likely to affect assessment of these outcomes. Standardisation of assessment
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	Active and systematic surveillance and clear participants flow diagram. However, more participants lost to follow-up in the hemiarthroplasty group (4 (21%) versus 1 (8%)). There are also some incorrect percentages that give rise to concern
Incomplete outcome data (attrition bias) Death, reoperation	Low risk	Active and systematic surveillance and clear participants flow diagram. It is likely that patients with complications would have returned
Selective reporting (reporting bias)	Low risk	No protocol. However, systematic data collection and reporting of all outcomes
Balance in baseline characteristics?	Unclear risk	Where reported, the baseline characteristics were balanced in the two groups. However, the baseline distribution of the fracture types, which included three 4-part fracture dislocations, was not reported
Free from performance bias?	Low risk	"All patients underwent surgery performed by 1 of 2 orthopedic surgeons (M.C., S.L.), both experienced in shoulder surgery." Same rehabilitation.

Fialka 2008

Methods	Method of randomisation: referral to random list and randomisation timed at surgery Assessor blinding: no Loss to follow-up at 1 year: 5/40 (3 deaths, 2 lost to follow-up)
Participants	Vienna General Hospital, Austria Period of study recruitment: not stated - lasted 22 months 40 patients with acute 4-part (Neer) proximal humeral fractures (type C: AO/ASIF classification), aged > 50 years, no history of previous problems in either shoulder, informed consent Exclusion criteria: concomitant vascular or neurological injuries of involved limb; prior operative procedures; neurologic or mental disorders; or drug abuse 30 female, 10 male; mean age 75 years; of 35: range 56 to 88 years
Interventions	Surgery started 7.3 days of injury (0 to 26 days). General anaesthesia used in all cases. Stems were cemented in place and bone grafting was performed using cancellous bone from patient's humeral head. 1. Hemiarthroplasty using EPOCA prosthesis (Argomedical). Fixation of tuberosities using wire cables threaded through a medial and lateral hole in the stem. 2. Hemiarthroplasty using HAS prosthesis (Stryker). Fixation of tuberosities using transosseous braided sutures tied to lateral fin of the stem. Same general rehabilitation protocol used for both groups: shoulder kept for 2 weeks in immobiliser to prevent active external rotation, passive movement for 15 minutes per day by physiotherapist to avoid contractures and shoulder stiffness. Then, active range of motion increased to horizontal level. Active external rotation initiated after another 2 weeks. Assigned: number in each group not known Completed (at 1 year): 18/17
Outcomes	Length of follow-up: 1 year; also assessed at 12 days, 3 & 6 weeks, and 6 months Functional assessment (individual Constant score, where results were relative to patient's unaffected shoulder) Range of motion (active forward flexion, abduction, external rotation) Radiological assessment: resorption of tuberosities, superior migration of prosthesis, anterior subluxations, glenoid erosion, aseptic stem loosening, secondary dislocation of the tuberosities, heterotopic ossification Deep infection Periprosthetic fracture Reoperation & scheduled for reoperation (persistent pain) Mortality
Notes	Differences between the two prostheses include the type and position of fixation of the tuberosities and the volume of the stem in the metaphyseal area, thus allowing different amounts of additional (autologous) cancellous bone grafting. The data for heterotopic ossification were contradictory and not used here. Request for information sent to contact trialist on 19 February 2010

Risk of bias

Bias	Authors' judgement	Support for judgement

Fialka 2008 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	"The random list was designed to finally produce 2 groups of equal size."
Allocation concealment (selection bias)	Unclear risk	"Each surgeon was informed at the beginning of the operation as to which implant had randomly been selected."
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	No blinding.
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Lack of blinding unlikely to affect assessment of these outcomes. Standardisation of assessment
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	High risk	The group allocation and baseline data were not provided for 5 participants: 2 lost to follow-up and 3 who had died. Standard deviations not provided
Incomplete outcome data (attrition bias) Death, reoperation	Unclear risk	Group allocation not provided for those who had died.
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge this.
Balance in baseline characteristics?	Unclear risk	Incomplete baseline data (5 excluded) to confirm baseline comparability of those in analysis
Free from performance bias?	Low risk	No indication of performance bias: a "general rehabilitation protocol was used for all patients regardless of the type of implant. "; each of the 4 participating surgeons was experienced in joint replacement surgery

Fjalestad 2010

Methods	Method of randomisation: use of computer software by independent hospital statistician; block size 12; use of numbered opaque sealed envelopes Assessor blinding: no, but assessment by two independent physiotherapists Loss to follow-up at 1 year: 2/50 (2 deaths); at 2 years: 8/50 (3 deaths)
Participants	Olso University Hospital, Oslo, Norway Period of study recruitment: May 2003 to May 2008 50 patients with displaced proximal humeral fractures, AO group B2 or C2 (displaced 3-part and 4-part fractures) who were admitted to hospital. Malposition was at least

	45° angular deviation in the true frontal (inclination) or transthoracic radiographic projections, regardless of whether the fracture was impacted or not. The greater or lesser tuberosity had to be displaced at least 10 mm. Furthermore, the displacement between the head and metaphyseal/diaphyseal main fragments should not exceed 50% of the diaphyseal diameter. Age 60 years or over. Written informed consent. Resident in Oslo. Exclusion criteria: non-Scandinavian ethnicity, previous history of injury or illness of the injured or contralateral shoulder, injury of the other part of the humerus or the contralateral upper extremity, alcohol or drug abuse, dementia or neurological disease or severe cardiovascular disease that would contraindicate surgery. 44 female, 6 male; mean age 73 years, range 60 to 88 years
Interventions	Interventions (and randomisation) started after hospital admission. (On admission to the hospital, all patients were immobilized in a modified Velpeau bandage.) 1. Surgery: operation occurred within the first week after admission to hospital. Open reduction and fixation using a minimally open deltopectoral approach with an interlocking plate device (Locking Compression Plate (LCP) of the AO basic type, Synthes, Switzerland) and metal cerclages to secure the tuberosities. Surgery was performed under fluoroscopic control. Then immobilisation in a modified Velpeau bandage until self-exercises and instructed physiotherapy was started on the third postoperative day. 2. Non-surgical treatment: all patients stayed in the hospital for at least 1 day and received the same instructions from the physiotherapist as those allocated to surgery. If the displacement between the head and metaphyseal fragment (main fragments) exceeded 50% of the diaphyseal diameter (subsequent to randomisation), closed reduction was performed in the operating room under general anaesthesia within 48 hours of admission. Immobilisation in a modified Velpeau bandage for 2 weeks before self exercises and instructed physiotherapy started on day 15. The same self-training programme and instructed physiotherapy programme used for both groups, although the non-surgical treatment group started 12 days later. Both groups progressed to strengthening exercises at the 6-week time point. Physical therapy and self-exercise were recommended for at least 6 months. Assigned: 25/25 Completed (at 1 year): 23/25
Outcomes	Length of follow-up: 2 years; also assessed at 2, 8, 12, 26 and 52 weeks Constant shoulder score (both shoulders) (3, 6, 12 & 24 months) ASES (American Shoulder and Elbow Surgeons) questionnaire (sports domains not included - maximum 24 points) (6, 12 & 24 months) Quality of life score: Harri Sintonen 15D instrument (sexual function domain not included) Mortality Fixation failure or redisplacement - subsequent operation Radiographic outcomes including avascular necrosis (score 2 = no changes; 1 = changes to normal trabecular organisation < 50% of humeral head; 0 = > 50% or partial collapse) ; and post-traumatic glenohumeral osteoarthritis Check for axillary nerve injury Health economic outcomes, including direct (cost of surgery; cost of hospital stays) and indirect costs (sick leave, family use of time to assist patient) Length of stay in acute hospital and hospital rehabilitation centre

Notes	Information on the trial received December 2006 from Dr Tore Fjalestad. Currently only some results for one year follow-up are published. Communication from Dr Tore Fjalestad in April 2010 indicated that the two-year follow-up was likely to be finished during 2010. Further information from Dr Tore Fjalestad in April 2012 indicated that the two-year follow-up had been submitted to another journal (estimated publication during 2012) More details on non-surgical treatment were provided in Fjalestad 2012. Tore Fjalestad also provided in an email (April 2012) the following clarification on the use of closed reduction for 8 non-surgically treated participants (this had not been described in the protocol): "The primary X-rays were assessed for classification and decision-making for closed reduction. Those eight patients had a new radiographic examination after allocation to non-surgical treatment and after the procedure in the operating room, to confirm an acceptable position of the fragments. If not acceptable, the patients had to be treated with ORIF. Surprisingly, only one patient demonstrated unacceptable re-displacement after two weeks, and was analyzed according to intention-to-treat principle in the non-surgical group at one year." Two-year follow-up results published in 2014 (Fjalestad 2014a).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The [randomisation] procedure was designed by the statistician at the hospital research centre using the computer software S-PLUS 6.0 for Windows 2002 ... Randomisation was based on equal blocks of length 12, with the exception of the last one, which was interrupted due to 50 patients."
Allocation concealment (selection bias)	Low risk	"Randomisation was performed by means of consecutively numbered and sealed non-translucent envelopes containing each participant's allocation to surgery or to non-surgical treatment." Independent statistician
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	Two trained physiotherapists performed the 15D interviews. The physiotherapists were not blinded to group assignment. No provider or participant blinding
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Lack of blinding unlikely to affect assessment of these outcomes, but may affect decisions for subsequent surgery

Fjalestad 2010 (*Continued*)

Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	Participant flow diagram provided and intention-to-treat analysis conducted However, reported in 2014: "Missing data were handled according to single imputation by the last observation for each individual." Also, some imbalance in loss to follow-up 2 (8%) (surgery) versus 6 (24%) (non-surgical)
Incomplete outcome data (attrition bias) Death, reoperation	Low risk	Participant flow diagram provided and intention-to-treat analysis conducted
Selective reporting (reporting bias)	Unclear risk	Trial registered after completion. Small discrepancies in trial inclusion criteria
Balance in baseline characteristics?	Unclear risk	Statistically non significant imbalance in gender (5 females versus 1 male) and baseline quality-of-life scores (higher in surgical group)
Free from performance bias?	Low risk	All the operations were performed by three surgeons experienced in the procedure performed

Hodgson 2003

Methods	Randomised using sequentially numbered sealed envelopes Assessor blinding: yes, on review of patients at home or clinic appointment Loss to follow-up at 1 year: 4 (1 death); at 2 years: 12 (3 deaths)
Participants	Royal Hallamshire Hospital, Sheffield, UK Period of study recruitment: November 1998 to April 2000 86 patients, over 40 years old, with minimally displaced 2-part fractures (Neer), including isolated fractures of the greater tuberosity Exclusion criteria: inability to understand written or verbal information 70 female, 16 male; mean age 70 years
Interventions	Intervention started: at arrival at A&E. 1. Early physiotherapy (within 1 week of the fracture). Most patients were seen by a physiotherapist at clinic the day after their fracture. Patients received a sling for comfort but were instructed to take their arm out of the sling and to perform gradual, assisted movements of the upper limb. 2. Late physiotherapy after 3 weeks of immobilisation in a collar and cuff sling. Both groups received same rehabilitation programme. First 2 weeks: education and instruction for home exercises; weeks 2 to 4: progression to full passive flexion and light functional exercises; week 4: start of progressive functional exercises. Discharge when both patient and physiotherapist thought independent shoulder function was achieved

Hodgson 2003 (*Continued*)

Outcomes	Length of follow-up: 2 years, also 8 and 16 weeks and 1 year Functional assessment (Constant score) Patients' perceived health status: SF36 (physical function, physical role limitation, pain) ; Croft shoulder disability questionnaire Complications Number of physiotherapy treatment sessions
Notes	Information on this trial received from Mr Hodgson on several occasions. This included draft report of the 2-year follow-up and notice of their plan to extend follow-up to 5 years

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No details: "using sequentially numbered sealed envelopes we randomly allocated patients"
Allocation concealment (selection bias)	Low risk	"using sequentially numbered sealed envelopes we randomly allocated patients". Also from phone conversation (08/08/2001): "physio opened envelopes when details entered on envelope"
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	Blinded assessor of function but patients and care providers were not blinded
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Lack of blinding unlikely to affect assessment of these outcomes
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Low risk	A full account of loss to follow-up provided. While 14% at 2 years (12/86), it was under 5% (4/86) at 1 year
Incomplete outcome data (attrition bias) Death, reoperation	Low risk	Participant flow provided.
Selective reporting (reporting bias)	Unclear risk	Trial registration was incomplete and differed slightly from final reports
Balance in baseline characteristics?	Unclear risk	More males in the early mobilisation group (11 versus 5).

Hodgson 2003 (*Continued*)

Free from performance bias?	Low risk	Performance bias seemed unlikely.

Hoellen 1997

Methods	Randomisation method unknown Assessor blinding: not stated Loss to follow-up at 1 year: 12/30 (3 deaths)
Participants	University Clinic Ulm, Germany Period of study recruitment: 1/12/1994 to 30/06/1996 in Hoellen 1997 report (to 31/08/1998 in Holbein 1999 report) 30* patients with 4-part fractures (Neer). *see Notes. Exclusion criteria: age < 65 years, > 14 days since fracture, rheumatoid arthritis, previous shoulder injury, terminally ill 24 female, 6 male; mean age 74 years
Interventions	Interventions started within 14 days of fracture. 1. Hemiarthroplasty (Global prosthesis, DePuy, US) - cemented 2. "Minimal osteosynthesis": tension band wiring - 2 pins + figure of 8 wire All were given low dose heparin for DVT prophylaxis. The same post-operative treatment was used in both groups. A Glichrist bandage was used for temporary rests. Passive moving exercises started from first postoperative day, with active exercises postponed until after 6 weeks. Referral to rehabilitation clinic for 3 to 4 weeks post discharge. Assigned: 15/15 Completed (1 year): 9/9
Outcomes	Length of follow-up: 1 year Functional assessment (Constant score) Mobility (component of Constant score) Pain (ditto) Power Haematoma Infection Implant failure Medical complications Re-operation Time on ward Discharge location Mortality
Notes	The plan for longer term follow-up was announced in the Hoellen 1997 trial report. Further abstracts and a trial report (Holbein 1999) were identified for the review update (Issue 4, 2003). Holbein 1999 reported on 39 patients (19 versus 20), with 3- and 4-part fractures, 31 (number in each group not known) of whom had been followed up for 1 year and 24 (number in each group not known) for 2 years. Requests (June 2003) for further information, including for denominators, resulted in the discovery that both Dr Holbein and Dr Hoellen were no longer at Ulm

Hoellen 1997 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No details: prospective randomised trial
Allocation concealment (selection bias)	Unclear risk	No details: prospective randomised trial
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	No blinding.
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Lack of blinding unlikely to affect assessment of these outcomes
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	High risk	Participant flow provided but large loss to follow-up (12/30 = 40%); and potential exclusions
Incomplete outcome data (attrition bias) Death, reoperation	Unclear risk	Participant flow provided but large loss to follow-up (12/30 = 40%). Serious outcomes though are less likely to be missed
Selective reporting (reporting bias)	High risk	Insufficient information to judge this but the pragmatic removal of the power component of the Constant score was post hoc. Also non addressed difference in trial inclusion criteria between the two reports of this trial
Balance in baseline characteristics?	Unclear risk	No information on baseline characteristics of the two treatment groups but inclusion criteria rule out some confounders
Free from performance bias?	Unclear risk	Same post-operative treatment but in all there is insufficient information to assess performance bias

Kristiansen 1988

Methods	Method of randomisation: unknown, "randomly selected" Assessor blinding: unlikely Loss to follow-up at 1 year: 10/31 (4 failed to attend, 2 died, 4 excluded)
Participants	Rigshospitalet, Copenhagen, Denmark Period of study recruitment: not stated 30 patients with 31 displaced 2-part (7 fractures), 3-part (19) and 4-part (5 fractures) proximal humeral fractures (Neer). Exclusion criteria: no information (of 31 fractures) 22 female, 9 male; age range 30 to 91 years
Interventions	Interventions started: not stated. 1. Surgery: Percutaneous reduction (using Steinmann pin under image intensifier control) and external fixation (2 half pins with continuous threads into humeral head and 2 or 3 pins into the humeral shaft, and neutralising bar applied; Steinmann pin removed) 2. Non-surgical treatment: closed manipulation under general anaesthesia & sling Assigned: 15/16 Completed (at 1 year): 11/10
Outcomes	Length of follow-up: 12 months; also assessed at 3 & 6 months 'Treatment failure': poor reduction, pin removal due to loosening Non-union Quality of fracture reduction: good, fair, poor Functional overall score: excellent, satisfactory, unsatisfactory, poor. Neer (without anatomical section) Complications: avascular humeral head necrosis, deep infection, radiographic pseudarthrosis, refracture Reoperations Mortality
Notes	In both groups, functional exercises were started under instruction during the first week. Excluded participants were: 1 treatment failure (deep infection) in the surgical group; and 2 treatment failures (poor reduction) and 1 refracture in the non-surgical treatment group

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No details: "randomly selected for treatment"
Allocation concealment (selection bias)	Unclear risk	No details: "randomly selected for treatment"
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	No blinding reported.

Kristiansen 1988 (*Continued*)

Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Unlikely to be affected by lack of blinding
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	High risk	Exclusion of data for participants with treatment failure and early refracture from 12 month review. Large loss to follow-up (10/31 = 32%)
Incomplete outcome data (attrition bias) Death, reoperation	Low risk	Participant flow provided.
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge this.
Balance in baseline characteristics?	Low risk	No information on the patient with bilateral fractures but a relatively minor unit of analysis issue
Free from performance bias?	Unclear risk	No information on operator competence/ expertise.

Kristiansen 1989

Methods	Method of randomisation: unknown Assessor blinding: yes at 2-year follow-up Loss to follow-up at 2 years: 46/85 (18 deaths, 28 non-attenders)
Participants	Hvidovre University Hospital, Denmark Period of study recruitment: 1983 85 patients with proximal humeral fractures; 74% minimally displaced (Neer). Exclusion criteria: no information 60 female, 25 male; median age 72 years (1 week group), 70 years (3 weeks group)
Interventions	Interventions started immediately or after closed or open manipulation. 1. One week immobilisation in sling and body bandage. 2. Three weeks immobilisation in sling and body bandage. At the end of immobilisation, instructions were given to perform Codman's pendulum exercises as well as active movements of the elbow and hand. Assigned: 42/43 Completed (at 2 years): 18/21
Outcomes	Length of follow-up: 2 years; also assessed at 1, 3, 6 & 12 months Overall score (Neer without anatomic section) Mobility: overall from Neer score (range of motion: flexion, extension, abduction, internal & external rotation) Function: overall from Neer score (strength, reaching, stability) Pain: overall from Neer score (none to disabling)

Kristiansen 1989 (*Continued*)

	Complex regional pain syndrome type 1 (this was referred to as reflex sympathetic dystrophy in the trial report)	
Notes	Post immobilisation for both groups: instructions given for Codman's pendulum exercises as well as active movements of elbow and hand	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No details: "Random allocation to immobilization for 1 to 3 weeks was performed"
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	Only claimed for outcome assessors at final follow-up: "The 2-year follow-up examination was blind, as the examiners had no knowledge of the period of immobilization."
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	No blinding but may not have affected appraisal of mortality (which was not split by treatment group)
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	High risk	Large loss to follow-up (46/85 = 54%). Numbers given for those available at follow-up but incompletely reported data: only medians
Incomplete outcome data (attrition bias) Death, reoperation	High risk	Although numbers given for those available at follow-up, only overall mortality data provided (extracted from graph)
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge this.
Balance in baseline characteristics?	Unclear risk	Although there appeared to be comparability between treatment groups in age and gender, the percentage of minimally displaced fractures (79% versus 70%: 33/42 versus 30/43) differed between the two groups and no information was available on the numbers who had open manipulation (thus entailing surgery)
Free from performance bias?	Unclear risk	Lack of information to judge on performance bias.

Lefevre-Colau 2007

Methods	Randomised using block randomisation (under supervision of a statistician) and telephone to an independent researcher with patient details. Assessor blinding: yes Loss to follow-up at 6 months: 10 (all had difficulties in travelling to the hospital for scheduled sessions)
Participants	Cochlin Hospital, Paris, France Period of study recruitment: October 2002 to March 2005 74 patients, over 20 years old, with non-operatively treated impacted ("stable") fractures, including 34 minimally displaced (1-part fracture); 16 2-part (surgical neck or greater tuberosity (1)); and 24 3-part (surgical neck and greater tuberosity) (Neer). (AO classification also given). Written consent. Exclusion criteria: pre-existing shoulder pathology, neurological upper limb disorder, indication for shoulder surgery, multiple injuries, high-energy trauma, or difficulties with language or unable to understand rehabilitation programme or other treatment information. 54 female, 20 male; mean age 63 years
Interventions	Intervention started within 72 hours after fracture. 1. Early mobilisation: active rehabilitation begun within 72 hours of fracture: 2-hour sessions supervised by a physiotherapist, 5 times a week. Progressing from physical techniques to manage pain, then passive motion, performed by physiotherapist, in a) abduction, with arm suspension and patient supine (session 1); passive range of motion in forward elevation with the patient in a lateral supine position (session 2), with addition of external rotation with the patient in a seated position at session 8. After 3 weeks, sessions occurred twice a week without arm suspension. Patients wore a sling between sessions for 4 to 6 weeks, depending on the level of pain. After 6 weeks, active range of motion was begun during weekly sessions. Strengthening began at 3 months in twice-monthly sessions. Patients underwent a total of 32 sessions. 2. Usual care, starting with 3 weeks of sling immobilisation. Then 2-hour sessions supervised by a physiotherapist 4 times a week for 4 weeks. Passive mobilisation in all planes without arm suspension was performed by physiotherapist. Patients kept their arm in a sling between sessions for 1 to 3 additional weeks, depending on pain level. Then sessions were scheduled 2 times weekly for 5 weeks. Active range-of-motion exercises began after 6 weeks. After 9 weeks of rehabilitation, sessions occurred twice monthly until 6 months. Each patient underwent a total of 33 sessions Patients used oral analgesics to manage pain. After 4 to 6 weeks, patients were advised to perform daily exercises at home. Patients were discharged from the study at 6 months
Outcomes	Length of follow-up: 6 months, also 6 weeks and 3 months Functional assessment (Constant score: split into subjective and objective components) Pain Patient satisfaction Range of motion: abduction, anterior elevation, lateral rotation Complications: non-union (0); fracture displacement (0); treatment (injection) for subacromial impingement syndrome Compliance
Notes	

Lefevre-Colau 2007 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Block randomization involved choosing randomly from among blocks of lengths 4 and 2 to prevent the risk of predictability."
Allocation concealment (selection bias)	Low risk	"After completion of the trial entry details, an independent researcher responsible for treatment allocation was contacted by telephone."
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	"Outcome measures were recorded by two physicians, including one of the authors (F. F.), who were blinded to the treatment assignments." However, care providers and participants were not blinded to allocation
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Not reported.
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	Data were unavailable for 10 participants (5 in each group) who were lost to follow-up because of difficulties in travelling to the hospital. Their characteristics were reported not to differ from those who attended
Incomplete outcome data (attrition bias) Death, reoperation	Unclear risk	Not reported.
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge this; retrospective trial registration
Balance in baseline characteristics?	Low risk	Good balance in baseline characteristics
Free from performance bias?	Low risk	Rehabilitation was standardised and "delivered by physiotherapists who were experienced in the field"

Livesley 1992

Methods	Method of randomisation: unknown, double-blind Assessor blinding: likely as code only broken at end of trial Loss to follow-up at 6 months: 3/48
Participants	Mansfield District General Hospital, Mansfield, UK Period of study recruitment: November 1988 to May 1990 48 patients with minimally displaced humeral neck fractures (all Neer Group 1); 4 had epiphyseal fractures Exclusion criteria: able to co-operate with treatment and attend daily therapy for the first 10 working days. 37 female, 11 male; age range 11 to 85 years
Interventions	Interventions started on average 8.6 days since injury, upon referral to physiotherapy department. 1. Pulsed high frequency electromagnetic field ('Curapulse'), 30 minutes/day for first 10 working days. (Intensity setting 3, pulse repetition frequency 35, maximum pulse power 300 watts.) 2. Dummy apparatus (deactivated machine). Assigned: 22/26 Completed (at 6 months): 21/24
Outcomes	Length of follow-up: 6 months; also assessed at 1 & 2 months No data provided in report Range of movement of glenohumeral & scapulothoracic joints Pain scores, at rest, on movement, analgesia requirement Muscle wasting and strength Overall functional assessment score Subjective opinion of treatment Overall estimation of treatment (a 'good result') Time to discharge
Notes	All patients received the same standardised physiotherapy regimen. No data provided in report for comparison between the two interventions

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No details provided: "patients were randomized into two groups"
Allocation concealment (selection bias)	Low risk	"double-blind", and randomisation code was only broken at end of the trial period to permit analyses
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	Low risk	"double-blind", use of sham control

Livesley 1992 (*Continued*)

Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	No report of these outcomes
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	High risk	Although loss to follow-up reported, no results were presented for the trial groups
Incomplete outcome data (attrition bias) Death, reoperation	Unclear risk	No report of these outcomes
Selective reporting (reporting bias)	High risk	Results not presented.
Balance in baseline characteristics?	Unclear risk	Baseline comparability. However, although the article claims "patients ... were referred to the physiotherapy department without delay", the ranges for average time from injury to start treatment were 0 to 17 days (active) and 0 to 27 days (sham)
Free from performance bias?	Unclear risk	"Standardized physiotherapy regimen". However, although the article claims "patients ... were referred to the physiotherapy department without delay", the ranges for average time from injury to start treatment were 0 to 17 days (active) and 0 to 27 days (sham)

Lopiz 2014

Methods	Method of randomisation: used sequentially numbered, opaque, sealed envelopes Assessor blinding: not done Loss to follow-up: 2 participants of the MultiLoc nail group were excluded (one died and one was lost to follow-up)
Participants	Cl nico San Carlos Hospital, Madrid, Spain Period of study recruitment: March 2011 and September 2012 54 patients with displaced Neer 2- or 3-part proximal humerus fractures Exclusion criteria: pathological or open fractures, 4-part fractures, concomitant fractures in the same upper limb, or the opposite and previous surgery on that shoulder. Lack of consent Of 52: 41 female, 11 male; mean age 70 years, range 38 to 89 years
Interventions	All had general anaesthesia and intrascalene block. Mainly minimally invasive (percutaneous) - small deltoid-splitting incision (5 were open reduction with extended superior incision) 1. MultiLoc proximal humeral nail (MPHN) (Synthes-DePuy, Solothurn, Switzerland)

	- a straight nail 2. Polarus humeral nail (Acumed LLC, Hillsboro, OR, USA) - a curved nail Postoperatively, patients were immobilised with a sling. Passive range-of-motion exercises were allowed 24 to 48 hours after surgery, followed as soon as possible by active-assisted motion Assigned: 28/26 Completed: 26/26 (mean 14 months)
Outcomes	Length of follow-up: mean 14 months (6 to 22 months); formally 1, 3, 6 and 12 months Constant score (categories excellent; good; satisfied; fair; poor) Constant score - adjusted for age and sex Physical tests to assess evidence of rotator cuff disease for entry point morbidity Non-union, protrusion of the osteosynthesis material (subacromial impingement or articular surface intrusion of the screws), final alignment of the healed fracture (malunion) Re-operation (hardware removal for complications; reverse arthroplasty) Length of operation Intraoperative complications (none) Length of hospital stay Mortality
Notes	Request for information sent to Dr Lopiz on 20 October 2014 requesting clarification on method of sequence generation, details on the 2 excluded participants, query on tuberosity involvement of 3-part fractures in the MultiLoc nail group, clarification on whether 1 of 2 participants had a reverse shoulder replacement and length of follow-up times for each group. No response received

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"assistant generated the random allocation sequence, which was concealed from the authors." "Patients were randomly assigned to 2 parallel groups, initially at a 1:1 ratio, " description raises the concern that the sequence may have been predictable (not random) in the early stages - but was probably OK
Allocation concealment (selection bias)	Low risk	"Randomization was carried out with use of sequentially numbered, opaque, sealed envelopes." "All patients were randomized by a research co-ordinator who was not involved subsequently in the study."

Lopiz 2014 (*Continued*)

Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	"The health care providers involved with subsequent patient care were not blinded to the treatment." No mention of independent or blinded outcome assessment
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	"The health care providers involved with subsequent patient care were not blinded to the treatment." However, it is unlikely that lack of blinding will affect the reporting of these outcomes
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	Variable follow-up with no confirmation of similar follow-ups in the two groups. Additionally, data lost from 2 participants in the Polarus nail group (1 died + 1 lost to follow-up)
Incomplete outcome data (attrition bias) Death, reoperation	Low risk	Data lost from 2 participants in the Polarus nail group (1 died + 1 lost to follow-up). Unlikely to bias the results
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge this. No protocol found.
Balance in baseline characteristics?	Low risk	Although baseline data were not presented for 2 participants in the MultiLoc nailing group, there were no major imbalances in baseline characteristics between the two groups: "No statistically significant differences were found between the 2 groups."
Free from performance bias?	Low risk	"All surgeries were performed by 1 of the 3 senior trauma surgeons in the unit." Post-operative care was the same in both groups.

Lundberg 1979

Methods	Method of randomisation: unknown Assessor blinding: no, but mention of independent assessors Loss to follow-up at 3 months: 0/42; not known for final assessment
Participants	Gavle, Sweden Period of study recruitment: not stated 42 patients with undisplaced proximal humeral fractures (all Neer Group 1) fixed with a sling; 13 had avulsion of the greater tuberosity. Exclusion criteria: no information

Lundberg 1979 (*Continued*)

	37 female, 5 male; mean age 65 years
Interventions	Interventions started 7 days post injury, after removal of sling. 1. Instructed self-exercise: patients instructed to train 5 to 10 minutes, 4 to 5 times daily. They had 3 visits (day 1, and 1 & 3 months) to physiotherapist for instructions and checks. At 1 month, patients were told how to extend their exercises to same level as in physiotherapy group. 2. Conventional physiotherapy: 9 visits (average 20 to 30 minutes) between 2 to 3 months; patients encouraged to continue exercise at home. At about 4 weeks, treatment was intensified. Assigned: 20/22 Completed (at 3 months): 20/22; (at mean 16 months): number in each group not known
Outcomes	Length of follow-up: > 1 year (mean 16 months); also assessed at 1 & 3 months Range of movement: abduction, shoulder elevation - active & passive Pain (insignificant, moderate, severe), longstanding Lifting power of shoulder Frozen shoulder (secondary) Neer score (at final evaluation) including failure category Hand grip strength
Notes	No indication in the report of any loss to follow-up at last follow-up (> 1 year), but cannot be assumed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details of method: "In all, 42 patients were randomly assigned into two groups."
Allocation concealment (selection bias)	Unclear risk	No details of method: "In all, 42 patients were randomly assigned into two groups."
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	No blinding, although independent assessment claimed: "Examination was made by physicians and physiotherapists independently at 1 month and 3 months.."
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Not reported.
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	Full data provided for 1 and 3 months follow-up; but denominators not stated for long-term (mean 16 months) follow-up

Lundberg 1979 (*Continued*)

Incomplete outcome data (attrition bias) Death, reoperation	Unclear risk	Data not reported for these outcomes
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge this.
Balance in baseline characteristics?	Low risk	No major imbalances in baseline characteristics
Free from performance bias?	Low risk	No indications of performance bias.

Ockert 2010

Methods	Method of randomisation: used closed envelopes Assessor blinding: unknown Loss to follow-up (**2010 publication**): 10 patients excluded from analysis following randomisation; 6 with polytrauma, 2 with neurologic deficiency and 2 (1 versus 1) who were converted to shoulder arthroplasty intraoperatively. There was no mention of group allocation at randomisation or evaluation in the paper - these (8 versus 2) were notified after contact with the lead trial investigator Loss to follow-up (**2014 publication**): not stated
Participants	Ludwig-Maximilians University, Munich, Germany Period of study recruitment: August 2006 to July 2008 (extended to February 2010 for 2014 publication) **2010 publication:** 76 patients, aged over 18 years, with displaced proximal humeral fractures with displacement > 1 cm and angulation of fragments > 45 degrees (Neer criteria) Exclusion criteria: poly-traumatised patients, neurologic deficit or intra-operative conversion to shoulder arthroplasty. (Paper noted there were no open or pathological fractures.) Of 66: 48 female, 18 male; mean age 68 years, range 29 to 92 years **2014 publication:** 124 patients with displaced proximal humeral fractures with displacement > 1 cm and angulation of fragments > 45 degrees (Neer criteria) Exclusion criteria: open or pathological fractures, poly-traumatised patients, primary nerve palsy (given as examples) 89 female, 35 male; mean age 71 years, range not given
Interventions	1. Polyaxial angular stable plate fixation (Non-contact bridging - Proximal Humerus (NCB-PH)). Polyaxial plating allows a range of 0 to 15-degree angle off-centre. After insertion, a threaded screw cap locks the axis of the screw. 2. Monoaxial angular stable plate fixation with Proximal Humeral Internal Locking System (PHILOS) Synthes GmbH. Monoaxial locking plate technique is characterized by fixed divergent and convergent screw orientation due to threaded screw holes A deltopectoral approach was used for open reduction and internal fixation of all fractures. All patients received prophylactic intravenous antibiotic immediately before surgery. "The postoperative rehabilitation protocol included immediate passive- and active-assisted range of motion (ROM) up to 60-degree angle of abduction and elevation without forced external rotation for 6 weeks. Full ROM with active exercises was started 6 weeks

	after operation." (2010 publication) Assigned: 39/37 (2010 publication); 58/66 (2014 publication but post-randomisation exclusions may have occurred) Completed: 29/37; 58/66 (2014 publication)
Outcomes	**2010 publication:** Length of follow-up: 6 months (X-rays 1 day, 6 weeks, 3 months and 6 months) Secondary varus displacement (> 10 degrees) Delayed union (due to osteonecrosis) Intra-articular screw cut out Re-operation: revision surgery and early hardware removal Infection (none) Neurovascular injuries (none) **2014 publication:** Length of follow-up: 12 months (X-rays 1 day, 6 weeks, and 3, 6 and 12 months) Revision surgery (reasons given: secondary varus displacement, subacromial impingement, intra-articular screw cut out, infection) Screw position in different region of the humeral head
Notes	Request for information sent to Dr Ockert on 2 June 2012. Repeated on 8 June 2012, in email Peter Biberthaler regarding identification and further information on ongoing trial referred to in conference abstract (Biberthaler 2009) - it seems highly likely that the ongoing trial was this trial. However, this was not clear from email from Ben Ockert on 18 June 2012; this also provided details on the method of randomisation, the numbers allocated and analysed in each group The **2014 publication** of this trial (Ockert 2014) reported on an additional 48 participants, reflecting an extended period of trial recruitment, and a longer follow-up. Only the revision surgery data from Ockert 2014 were used in this review.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"consecutive patients ... were prospectively randomized". No description of sequence generation
Allocation concealment (selection bias)	Unclear risk	"consecutive patients ... were prospectively randomized". Contact from trialist revealed they "used closed envelope technique for randomization". (Exclusion criteria appeared to be applied post-randomisation.) **2014 publication:** "Randomization was performed by closed envelope technique."
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical out-	High risk	No mention of blinding. Radiographic assessment performed by two trained radiologists twice in separate sessions 8 weeks

comes, complications		apart. Consensus decision for osteonecrosis and implant-related failure. Criteria for healing stated
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	No mention of blinding, but unlikely to affect this.
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	High risk	"Follow-up rate was 71% of all radiographs taken 1 day, 6 weeks, 3 months, and 6 months after surgery." Numbers of patients allocated or assessed by intervention group provided after personal communication. Post-randomisation exclusions (10/76 = 13%),was imbalanced (8 versus 2) and other loss to follow-up not accounted for **2014 publication:** Concerns on post-randomisation exclusions continue for this publication
Incomplete outcome data (attrition bias) Death, reoperation	Unclear risk	As above. Paper described cases of revision surgery and early removal of metalwork; however, group allocation not given. Information provided subsequently
Selective reporting (reporting bias)	High risk	No protocol available. The extension of the recruitment, incomplete results and lack of full listing of exclusion criteria are of concern in the Ockert 2014 publication.
Balance in baseline characteristics?	Unclear risk	"The fracture types were equally distributed in both study groups." However, this applied to 66 participants. Does not state how many patients in each group or compare demographics Age and gender were comparable in the two groups in the Ockert 2014 publication. There was no mention of fracture type.
Free from performance bias?	Low risk	Six experienced surgeons performed the surgery: "In advance of this study, all surgeons were trained in the respective monoaxial and polyaxial locking plate system" Same antibiotic regimen and post-op management.

Olerud 2011a

Methods	Method of randomisation: opaque, sealed envelopes Assessor blinding: no, but mention of independent surgeon Loss to follow-up at 24 months: 7/60 (1 excluded themselves; 2 lost; 4 died)
Participants	Stockholm Söder Hospital, Stockholm, Sweden Period of study recruitment: April 2003 to March 2008 60 patients with acute displaced (based on Neer's criteria) 3-part proximal humeral fractures (all had displaced surgical neck fracture, all bar one had a displaced greater tuberosity; the exception had a displaced lesser tuberosity). Age 55 or older with a fracture sustained after a low-energy trauma (e.g. a simple fall). Independent living conditions Exclusion criteria: patients with a completely displaced shaft in relation to the head fragment or with a valgus impact fracture. Institutionalised, severe cognitive dysfunction (< 3 correct answers on a 10-item Short Portable Mental Status Questionnaire). Of 59 (1 patient excluded themselves): 48 female, 11 male; mean age 74 years, range 56 to 92 years (operations were performed within a mean of 6 (SD 4.1) days after the injury)
Interventions	Interventions (and randomisation) started after hospital admission. 1. Surgery: operation occurred at mean of 6.1 days of injury. Open reduction and fixation using a deltopectoral approach with a PHILOS plate (Synthes, Stockholm, Sweden) and with nonabsorbable sutures used to fix displaced/unstable lesser and/or greater tuberosity fractures. The reduction and position of the implant was checked with the aid of an X-ray image intensifier. (All patients had pre-operative antibiotics.) Post surgery, the arm was placed in a sling and patients were referred to a physiotherapist. The sling was used for 4 weeks; afterwards, the patients were allowed to use it at their own convenience. Pendulum exercises and passive elevation/abduction up to 90 degrees were started from the first postoperative day. After 4 weeks, the patients were allowed a free active range of movement. 2. Non-surgical treatment: arm immobilisation in a sling for 2 weeks, after which they were allowed to use it at their own convenience. After 2 weeks, the patients were referred to a physiotherapist, and pendulum exercises and passive elevation/abduction up to 90 degrees were started. After 4 weeks, they were allowed a free active range of movement. Assigned: 30/30 Completed (at 2 years): 27/26
Outcomes	Length of follow up: 2 years Constant shoulder score (both shoulders) DASH (Disabilities of the Arm, Shoulder and Hand) questionnaire Quality of life score: EQ-5D Mortality Pain Range of motion: abduction, flexion Fixation failure, redisplacement, non-union, malunion Subsequent surgery (reasons including deep infection, etc) Radiographic outcomes including avascular necrosis and osteoarthritis
Notes	Trial run concurrently with Olerud 2011b. Additional information on randomisation and trial location obtained from Dr Olerud (April 2012). Pain data received May 2012

Olerud 2011a (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"After clearance by an anesthetist, the patients were randomized (independently prepared opaque, sealed envelopes) to open reduction and internal fixation with a locking plate or nonoperative treatment." trial report "the patients were randomised by numbered sealed opaque envelopes drawn consecutively The envelopes were independently prepared and thoroughly mixed. After that the envelopes were numbered by another person. At the time of randomisation the envelopes were drawn in numerical order." personal communication
Allocation concealment (selection bias)	Low risk	See above
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	No assessor blinding, although "The final 24-month follow-up was performed by an independent orthopaedic surgeon not previously involved in the treatment." No provider or participant blinding.
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Lack of blinding unlikely to affect assessment of these outcomes, but may affect decisions for subsequent surgery
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Low risk	"In the outcome analyses, all patients remained in their randomization group regardless of secondary procedures according to the intention-to-treat principle." Participant flow provided; no cause for concern
Incomplete outcome data (attrition bias) Death, reoperation	Low risk	As above.
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge this. No protocol found.
Balance in baseline characteristics?	Low risk	No imbalances: baseline comparability.

Olerud 2011a (*Continued*)

Free from performance bias?	Low risk	"All operations in patients randomized to surgery were performed by 1 of 2 orthopaedic surgeons, both well experienced in shoulder surgery." While all surgical patients were referred to a physiotherapist after their surgery and non-surgically treated patients were referred after 2 weeks, this was unlikely to influence results. Otherwise, similar exercise / rehabilitation schedules

Olerud 2011b

Methods	Method of randomisation: opaque, sealed envelopes Assessor blinding: no, but mention of independent surgeon Loss to follow-up at 24 months: 6/55 (1 lost; 5 died)
Participants	Stockholm Söder Hospital, Stockholm, Sweden Period of study recruitment: April 2003 to March 2008 55 patients with an acute displaced (based on Neer's criteria) 4-part proximal humeral fractures (all had displaced surgical neck, greater and lesser tuberosity fractures). Age 55 or older with a fracture sustained after a low-energy trauma (e.g. a simple fall), no previous shoulder problems. Independent living conditions. Exclusion criteria: patients with a completely displaced shaft in relation to the head fragment or with a valgus impact fracture. Institutionalised, severe cognitive dysfunction (< 3 correct answers on a 10-item Short Portable Mental Status Questionnaire). 47 female, 8 male; mean age 77 years, range 58 to 92 years
Interventions	Interventions (and randomisation) started after hospital admission. 1. Surgery: operation occurred at mean of 6.0 days of injury. Humeral head replacement using a deltopectoral approach with the Global Fx prosthesis (DePuy, Sollentuna, Sweden); this is a modular prosthesis with a fixed angle and a conventional head - it has 3 fins. Heavy nonabsorbable sutures were tagged on the bone tendon interface of both tuberosities Cancellous bone graft from the head fragment was placed between the shaft and the tuberosities. (All patients had pre-operative and 2 doses post-operative antibiotics.) Post surgery, the arm was placed in a sling and patients were referred to a physiotherapist. The sling was used for 6 weeks; afterwards, the patients were allowed to use it at their own convenience. Pendulum exercises and passive elevation/abduction up to 90 degrees were started from the first postoperative day. After 6 weeks, the patients were allowed a free active range of movement. Strengthening exercises were begun after 3 months. 2. Non-surgical treatment: arm immobilisation in a sling for 2 weeks, after which they were allowed to use it at their own convenience. After 2 weeks, the patients were referred to a physiotherapist, and pendulum exercises and passive elevation/abduction up to 90 degrees were started. After 4 weeks, they were allowed a free active range of movement. Assigned: 27/28 Completed (at 2 years): 24/25

Outcomes	Length of follow up: 2 years Constant shoulder score (both shoulders) DASH (Diasabilities of the Arm, Shoulder and Hand) questionnaire Quality of life score: EQ-5D Mortality Pain Range of motion: abduction, flexion Fixation failure, redisplacement, non-union, malunion Subsequent surgery (reasons including non-union, etc) Radiographic outcomes including avascular necrosis and osteoarthritis
Notes	Trial run concurrently with Olerud 2011a. Additional information on randomisation and trial location obtained from Dr Olerud (April 2012). Pain data received May 2012

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"After clearance by an anesthesiologist, the patients were randomized (opaque sealed envelopes prepared independently) to a primary HA or nonoperative treatment." trial report "the patients were randomised by numbered sealed opaque envelopes drawn consecutively The envelopes were independently prepared and thoroughly mixed. After that the envelopes were numbered by another person. At the time of randomisation the envelopes were drawn in numerical order." personal communication
Allocation concealment (selection bias)	Low risk	See above
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	No assessor blinding, although "The final 24-month follow-up was performed by an independent orthopaedic surgeon not previously involved in the treatment." No provider or participant blinding.
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Lack of blinding unlikely to affect assessment of these outcomes, but may affect decisions for subsequent surgery

Olerud 2011b (*Continued*)

Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Low risk	"In the outcome analyses, all patients remained in their randomization group regardless of secondary procedures according to the intention-to-treat principle." Participant flow provided; no cause for concern
Incomplete outcome data (attrition bias) Death, reoperation	Low risk	As above.
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge this. No protocol found.
Balance in baseline characteristics?	Low risk	No imbalances: baseline comparability.
Free from performance bias?	Unclear risk	"In patients randomized to surgery, all operations were performed by 1 of 2 orthopedic surgeons, both well experienced in shoulder surgery ..." While all surgical patients were referred to a physiotherapist after their surgery and non-surgically treated patients were referred after 2 weeks, this was unlikely to influence results. As was the differences in timing for free ROM (6 versus 4 weeks). However, it was only reported for the surgical group that strengthening exercises were begun after 3 months

ProFHER 2015

Methods	Method of randomisation: remote randomisation computer programme with 1:1 allocation, stratifying by tuberosity involvement (yes or no) and using random block sizes of 4, 8, and 12 Assessor blinding: no, except for blinded independent coding Loss to follow-up at 24 months: 32/250 (12 no response, 6 withdrew (+ 1 who died), 14 died)
Participants	33 acute UK National Health Service hospitals, UK Period of study recruitment: September 2008 and April 2011 250 patients aged 16 years or older presenting within 3 weeks after sustaining a displaced fracture of the proximal humerus that involved the surgical neck. The degree of displacement had to be sufficient for the treating surgeon to consider surgical intervention but did not have to meet the displacement criteria of Neer (1 cm or 45° angulation of displaced parts, or both) for inclusion in the trial. Written consent Exclusion criteria: patients who had associated dislocation of the injured shoulder joint, open fracture, insufficient mental capacity to understand the trial or instructions for rehabilitation, co-morbidities precluding surgery or anaesthesia, clear indication for surgery such as severe soft-tissue compromise, multiple injuries (upper limb fractures), patho-

ProFHER 2015 (*Continued*)

	logical fracture (other than osteoporotic), terminal illness, or not resident in the hospital catchment area 192 female, 58 male; mean age 66 years, range 24 to 92 years
Interventions	Interventions (and randomisation) started after presentation at the hospital 1. Surgery: either internal fixation, such as with plate and screws (majority were Philos plates),or joint replacement (hemiarthroplasty). 2. Non-surgical treatment: patients were given a sling for the injured arm for as long as deemed necessary (3 weeks was suggested), followed by active early rehabilitation Delivery of care and rehabilitation, which was freely available for all patients, incorporated three set measures to ensure good standards of care within the NHS: provision of an information leaflet on personal care during sling immobilisation; a basic treatment protocol to guide physiotherapy; and promotion of home exercises. Rehabilitation care was provided by physiotherapists in inpatient, outpatient and/or community settings
Outcomes	Length of follow-up: 2 years, also 3 (for EQ-5D), 6 and 12 months Oxford Shoulder Score SF-12 (12-item short form health survey) Euroqol (EQ-5D) Complications, including surgical complications (wound infection, implant failure, shoulder dislocation, septicaemia); early medical complications, i.e. chest infection, confirmed myocardial infarction or stroke, treated deep vein thrombosis and pulmonary embolism Mortality Subsequent referral for operation or substantive treatment Data for economic evaluation: NHS and societal costs
Notes	Published protocol.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Randomization was done with a computer programme using 1:1 allocation, stratifying by tuberosity involvement (yes or no) and using random block sizes of 4, 8 and 12."
Allocation concealment (selection bias)	Low risk	"research associates randomly allocated individual patients to surgical or non-surgical treatment using an independent remote randomization service"
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	"There was no blinding of trial participants, clinicians, or assessment of outcomes." "Coding was performed by at least 2 independent coders blinded to treatment allocation." Discussion: "Although lack of blinding of

		patient-reported outcome assessment is unavoidable, similarities in the 2 groups in patient return of questionnaires and baseline characteristics at 24 months, and the lack of a significant effect of baseline patient preferences on the OSS results suggest this did not introduce a bias."
Blinding (performance bias and detection bias) Death, reoperation	Low risk	As above. Additionally, lack of blinding unlikely to affect assessment of these outcomes
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Low risk	Loss to follow-up balanced in the two groups. Trial reports: "Overall, 41 patients (16%) had missing follow-up data on at least 1 time point. Using complete data derived by multiple imputation resulted in comparable treatment effect estimates to the primary analysis with no overall statistically significant group difference (P = .48) . ..... Nonresponse (none or intermittent) was not associated with any demographic or fracture characteristics."
Incomplete outcome data (attrition bias) Death, reoperation	Low risk	Very high return of hospital forms: 249 of 250 (99.6%) at 1-year follow-up forms and 234 of 250 (93.6%) 2-year (but 2-year forms not sent for those who had already died before 1 year)
Selective reporting (reporting bias)	Low risk	Prospective trial registration, publication of trial protocol and trial analysis plan
Balance in baseline characteristics?	Low risk	The baseline characteristics were well balanced except for smoking status (there were more smokers in the non-surgical group). However, this was shown not to impact on the results
Free from performance bias?	Low risk	"It was emphasized that good standards care, both surgical and nonsurgical, should be provided throughout the treatment pathway for the injury, including surgical care or management of the sling, postoperative care, and rehabilitation in both groups. Participating hospitals did not introduce new or experimental interventions for these fractures during the study." "To avoid learning curve problems, sur-

		geons and physiotherapists used surgical interventions and procedures with which they were familiar." "Physiotherapy treatment log data demonstrated equal access and implementation between groups,with similarly high numbers of participants recorded as performing home exercises in both groups."

Revay 1992

Methods	Randomisation from closed envelopes Assessor blinded Loss to follow-up at 1 year: 1/48
Participants	Danderyd Hospital, Danderyd, Sweden Period of study recruitment: not stated 48 patients with 2-, 3- or 4-part minimally displaced proximal humeral fractures (< 1 cm or < 45 degrees; Neer Group 1) treated non-surgically with sling immobilisation for 1 week. Exclusion criteria: patients with skin diseases and/or chlorine allergy, non-ambulatory 39 female, 9 male; mean age 66 years
Interventions	Interventions started 5 to 10 days post-injury after removal of sling. 1. Swimming pool training (30 minutes each session, up to 20 sessions maximum) in groups (6 to 8 patients) plus instructions for self-training (see below). 2. Instructions for self-training: exercises to be performed at least 4 times a day for 10 to 15 minutes each time, use of hand on injured side for activities of daily living, advice on relaxation and resting positions. Assigned: 25/23 Completed: number in each group not known
Outcomes	Length of follow-up: 1 year; also assessed at 3 weeks, 2 & 3 months Pain (analogue scale) Activities of daily living: subjective assessment of 9 activities each rated on a 5 point scale Functional scale: 6 point scale Joint movement (abduction, flexion, internal rotation)
Notes	Means (probably) presented without standard deviations.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No details: "patients were randomized into two groups"

Revay 1992 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Insufficient details of safeguards: "randomized and given instructions in a sealed envelope"
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	"All patients were examined by a physiotherapist who did not know which group each patient belonged to". However, no participant or care provider blinding nor mention of ways to prevent disclosure to assessor
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Not reported.
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	High risk	The treatment group of the participant lost to follow-up was not stated. Standard deviations not provided. Graphs only provided for female participants - denominators not provided for these
Incomplete outcome data (attrition bias) Death, reoperation	Unclear risk	Not reported. The treatment group of the participant lost to follow-up was not stated
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge this.
Balance in baseline characteristics?	Unclear risk	Baseline data not provided for gender.
Free from performance bias?	Unclear risk	Uncertainty if any compensatory advice given for the control group

Rommens 1993

Methods	Method of randomisation: alternation Assessor blinding: unlikely Loss to follow up at 3 weeks: 0/28
Participants	Leuven University Hospital, Belgium Period of study recruitment: 1991 28 patients with acute 2- and 3-part proximal humeral fractures (but most were non or minimally displaced). Exclusion criteria: those indicated for surgical intervention, age < 15 years, with multiple injuries or other fractures at same site 22 female, 6 male; mean age 69 years, range 25 to 100 years
Interventions	Interventions started immediately. 1. Gilchrist bandage, 2 to 3 weeks. The arm was bandaged with mesh type tubing and held by two slings: one round the shoulder and neck and the other which immobilised

Rommens 1993 (*Continued*)

	the distal part of the upper arm. (Bandage allowed wrist and hand exercises.) 2. Desault bandage, 2 to 3 weeks. Arm was immobilised to the chest using a circular elastic body bandage. (Some had one or more strips of plaster to stop the bandage slipping.) Assigned: 14/14 Completed (at fracture consolidation): 14/14
Outcomes	Length of follow-up: until fracture consolidation; also assessed at 1 & 3 weeks Functional results: overall result, no data Pain: patient questionnaire, 0 (none) to 100 (significant) scale Displacement of fracture Complication: skin irritation Removal of bandage Surgeon assessment of ease of application of bandage Patient assessment of bandage
Notes	Two fractures in the Gilchrist group required reduction. Seven participants had other fractures: 3 in group 1 (2 rib, 1 vertebra); 4 in group 2 (1 ankle, 1 hip, 1 rib, 1 vertebra) Trial reports in German; translation obtained.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quasi-randomised: alternation
Allocation concealment (selection bias)	High risk	Alternation
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	No mention of blinding
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Not reported
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	While all participants were followed up and intention-to-treat analyses seemed to have been done, no data on function were presented nor were the criteria for judging fracture consolidation
Incomplete outcome data (attrition bias) Death, reoperation	Unclear risk	Not reported
Selective reporting (reporting bias)	High risk	Insufficient information to judge this, but data not provided on function

Rommens 1993 (*Continued*)

Balance in baseline characteristics?	Unclear risk	Small discrepancies (e.g. in other injuries or having fracture reduction) can have bigger consequences for small group sizes
Free from performance bias?	Unclear risk	Differences in care programmes cannot be ruled out.

Sebastiá-Forcada 2014

Methods	Method of randomisation: sequentially numbered opaque sealed envelopes Assessor blinding: yes, independent surgeons who did not know which type of prothesis was used Loss to follow-up at minimum 24 months: 1/62 (1 died)
Participants	Hospital Universitario de Elda, Elda, Alicante, Spain Period of study recruitment: 2009 to 2011 62 older patients with acute complex proximal humeral fractures (Neer's: 3-part, 4-part and 4-part + dislocation). Age > 70 years. Candidate for shoulder arthroplasty: indications for shoulder arthroplasty were complex fractures not amenable to reconstruction, including displaced 4-part fractures, fracture-dislocations with 3-part fractures, and head-splitting fractures with more than 40% articular surface involvement. (All had computed tomography.) Informed consent. Exclusion criteria: contraindications to surgery, prior surgery in the shoulder, associated ipsilateral upper limb fracture and neurologic disorder 53 female, 9 male; mean age 74 years, range 70 to 85 years (operations were performed within a mean of 5.1 (range 1 to 12) days after the injury)
Interventions	A modular shoulder replacement system (SMR; Lima, Udine, Italy) was used in both groups. The system allows the choice of cementless shoulder prostheses: hemiarthroplasty, reverse and anatomic arthroplasty). A common cementless humeral stem with porous coating titanium was assembled with one of two prostheses. The same deltopectoral approach and basic surgical technique was used at each shoulder; the tuberosities were repositioned as anatomically as possible and reattached with nonabsorbable sutures. Regional anaesthesia. In both groups, a suction drain was placed postoperatively for 24 hours. Standard antibiotic and antithrombotic prophylaxis was given 1. Reverse shoulder arthroplasty (RSA): an SMR Reverse prosthesis was used in all shoulders. Of note is that the reverse liner of polyethylene (cross-link) had a chamfer in its inferior portion designed to decrease the risk of impingement and the consequent scapular notching. The proximal humeral body was in titanium alloy with a hole to allow suture of the tuberosities. Shoulders were postoperatively immobilised in sling for 2 weeks in a regimen similar to that of the HA group. Patients then continued with physiotherapy in a rehabilitation centre for at least 4 weeks to perform deltoid activation exercises and activities as tolerated 2. Hemiarthroplasty: an SMR Trauma prosthesis was implanted. The proximal humeral body had holes to allow suture of the tuberosities to the stem, and the modular head was in titanium alloy. Rotator cuff tears repaired if possible. Sling immobilisation after surgery, gradually discontinued around 3 weeks. Passive mobilisation and pendulum exercises were allowed immediately. At week 2, passive- and active-assisted exercises were

	allowed in a rehabilitation centre with forward elevation and abduction limited to 100º and external rotation limited to 30º. When consolidation of tuberosities was observed on the radiographs (around 6 weeks), active and resisted exercises were started Assigned: 31/31 Completed (at 2 years): 31/30
Outcomes	Length of follow-up: mean 28.5 months (range: 24 to 49 months); also followed-up but no data for 6 weeks, 3, 6 and 12 months (and then yearly) QuickDASH University of California-Los Angeles (UCLA) score Constant score (absolute and adjusted for age and gender) Mortality Complications (intra-operative fracture, infection, haematoma, neurological, severe stiffness, proximal migration of implant) Re-operations Range of motion (anterior forward; abduction) Tuberosity healing, malunion, non-union resorption Strength (not reported) Radiographs: acromiohumeral distance; scapular notching, loosening, heterotopic ossification, proximal migration, radiolucent lines
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Method not stated, although seems likely that an appropriate method was used
Allocation concealment (selection bias)	Low risk	"Randomization to the HA or RSA group was based on sequentially numbered opaque sealed envelopes. The surgeons were not involved in the randomization process."
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	"All postoperative functional evaluation forms were completed at each visit by an independent experienced surgeon (A.L.U.) who had not participated in the surgeries and did not know which type of prosthesis had been used" However, there was no blinding of care providers or participants
Blinding (performance bias and detection bias) Death, reoperation	Low risk	Surgeons were experienced. "clinical and radiologic evaluations were performed by independent observers who had not participated in the surgeries"

Sebastiá-Forcada 2014 (*Continued*)

Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Low risk	One loss to follow-up (death) only. Interim follow-up data not reported
Incomplete outcome data (attrition bias) Death, reoperation	Low risk	One loss to follow-up (death) only.
Selective reporting (reporting bias)	Unclear risk	No trial registration or published protocol. Marginal but some arbitrary definitions of outcomes. No data on interim follow-ups
Balance in baseline characteristics?	Unclear risk	Baseline characteristics were balanced in the two groups. (Characteristics of 1 participant not provided.) Difference in cuff tears between groups accounted for and tested
Free from performance bias?	Low risk	All operations were performed by 2 surgeons experienced in shoulder surgery; the modular shoulder replacement system was already in use at centre before the study. Same approach and operating methods and conditions; regional anaesthesia etc Comparable rehabilitation - differences appropriate for different procedures

Smejkal 2011

Methods	Method of randomisation: computer-generated block randomisation with sealed envelopes Assessor blinding: no mention in the paper Loss to follow-up: 4 lost to follow-up and 2 died of breast cancer during the study period
Participants	University Hospital in Hradec Králové, Czech Republic Period of study recruitment: January 2006 to January 2010 61 patients with AO type A2, A3, B1 and C1 (2-part and 3-part) proximal humerus fractures aged between 18 and 80 years able to give informed consent Exclusion criteria: open fracture, associated injury (AIS > 2), open growth plates, or patient's health would limit the extent of surgery Of 55: 45 females, 10 males; mean age 61 years, range 21 to 81 years
Interventions	Interventions started 0 to 24 days after injury. 1. Open reduction and internal fixation group: consisted of patients undergoing open reduction with angle-stable osteosynthesis using a PHILOS plate (Synthes, Switzerland) 2. Minimally invasive group: Zifko method of minimally invasive osteosynthesis with intramedullary K-wire ((Kirschner wire) insertion (distally inserted) - figure in article shows 8 wires inserted into humeral head along medullary canal Assigned: number in each group not known (total 61)

	Completed: 28/27
Outcomes	Length of follow-up: mean 2 years Days to operation Constant-Murley score (relative to healthy limb) Time to recover normal upper limb function Complications Time to radiographically assessed recovery Anatomical position X-ray exposure Length of operation Length of hospital stay
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"The patients were randomised to the groups by a computer programme which facilitates the maintenance of homogeneity of the groups compared." Web-based translation implied use of random numbers and permuted blocks so as to get similar numbers on each group. Produced independently by a statistical company
Allocation concealment (selection bias)	Low risk	The sealed envelopes were created by a professional statistical company (Pharm test s. r. o., Hradec Králové): in accordance with randomization sheet each envelope their number and sealed inside information," zifko" or "LCP." The sealed envelopes were opened sequentially
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	Not possible to blind patient/providers. No mention of outcome assessment
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	May not affect assessment
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	High risk	Incomplete data (and group of 6 excluded participants not noted)

Smejkal 2011 (*Continued*)

Incomplete outcome data (attrition bias) Death, reoperation	High risk	Incomplete data (and group of 2 deaths not stated)
Selective reporting (reporting bias)	Unclear risk	No protocol
Balance in baseline characteristics?	Unclear risk	Aside from age - no details or confirmation of this
Free from performance bias?	Unclear risk	No details - including of surgeon's experience

Soliman 2013

Methods	Method of randomisation: use of computer-generated random numbers table Assessor blinding: yes, blinded observer for Constant score, pain and range of motion Loss to follow-up: 8 post-randomisation exclusions
Participants	Cairo University Hospital, Cairo, Egypt Period of study recruitment: 2005 to 2009 45 patients treated with hemiarthroplasty for 4-part fractures of the proximal humerus, fracture dislocations or head splitting fractures presenting within the first five days after injury. Informed consent Exclusion criteria: not available. Exclusion criteria applied to post-randomisation exclusions of participants with complications 13 females, 32 males; mean age 52 years (of 37 participants), range 45 to 60 years (Note: This was a young population with very severe injuries. Predominantly males and presumably high-energy trauma. The biceps tendon is stronger in younger patients.)
Interventions	Interventions started within 5 days after injury. Same prosthesis (Johnson and Johnson) and surgical technique used in both groups. "A standard deltopectoral approach was used and the coracoacromial ligament was preserved in all patients." The operative technique is described at length in the article. 1. Hemiarthroplasty and tenodesis of long head of the biceps (LHB): LHB tendon was divided at its insertion and tenodesed by Ethibond sutures into the insertion of the pectoralis major 2. Hemiarthroplasty: LHB tendon left intact. Post-surgery, the arm was immobilised in a position of neutral rotation for 4 weeks. This was followed by the same physiotherapy protocol for all participants Assigned: 23/22 Completed (2 years): 19/18
Outcomes	Length of follow-up: mean 2 years (range 21 to 27 months) Constant score ("modified"; not clear how) Pain (VAS, then categorised to none, mild, moderate, severe) Re-operation Complications (these were excluded - see Notes) Anterior shoulder elevation

Notes	Post-randomisation exclusions: "Eight patients were excluded from the study within the first 3 months of follow-up due to tuberosity malposition (three patients), inferior subluxation of the prosthesis (two patients), loss of reduction of the greater tuberosity (two patients) and deep infection, which slowed down the physiotherapy protocol and required surgical debridement (one patient)." (page 262 in report) Contact with the lead author resulted in no clarification of the method of randomisation ("we enrolled the patients in a random number"), but information on the manufacturer of the implant, a breakdown of the numbers of participants with specific complications in each group and clarification that there were no re-operations aside from debridement for a deep infection

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Patients were randomly assigned to either hemiarthroplasty or hemiarthroplasty and tenodesis of the LHB, according to a computer-generated random number sequence. "
Allocation concealment (selection bias)	Unclear risk	"After enrolment, cases were sequentially arranged and plotted on the random number table to determine to which group they will be assigned" No mention of safeguards
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	Low risk	All patients were evaluated by a blinded observer using the Constant score
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Lack of blinding unlikely to affect reporting
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	High risk	Inappropriate exclusion of eight participants. Although the number of post-randomisation exclusions was four in each group, the loss to follow-up was 17% (4/23 in the tenodesis group) and 18% (4/22 in the intact LHB tendon group) and all eight participants were more likely to have had poor results
Incomplete outcome data (attrition bias) Death, reoperation	Low risk	Data from author clarified that only the participant with deep infection had subsequent treatment for a complication

Soliman 2013 (*Continued*)

Selective reporting (reporting bias)	High risk	Retrospective trial registration. Inadequate description of outcomes, including the categorisation of pain. Strength was measured but not reported. Pain categories and measurement not defined sufficiently
Balance in baseline characteristics?	Unclear risk	No separate data aside from age. While balanced for age, these data apply to 37 of 45 participants. No details on fracture severity and cuff integrity, both of which could affect result
Free from performance bias?	Low risk	Same surgeon operated with same prosthesis. Same post-surgical care and rehabilitation

Stableforth 1984

Methods	Method of randomisation: unknown, "randomly selected" Assessor blinding: unlikely Loss to follow-up at 18 months to 12 years: 2/32 (2 deaths)
Participants	Bristol Royal Infirmary, Bristol, UK Period of study recruitment: 1970 to 1981 32 patients with displaced 4-part proximal humeral fractures (Neer). Exclusion criteria: impacted or minimally displaced fractures 25 female, 7 male; mean age 68 years, range 52 to 88 years
Interventions	Interventions started: within 5 days for surgery. 1. Neer prosthesis, uncemented 2. Non-surgical treatment: closed manipulation All were placed in sling, mobilisation of hand encouraged, shoulder flexion rotation exercises after 2 to 3 days. Supervised physiotherapy for 3 to 6 months. Assigned: 16/16 Completed (at 1 year): 15/15 (but totals given as 16/16 in tables in the trial report)
Outcomes	Length of follow-up: stated as 18 months to 12 years; but also assessed regularly up to 6 months Dependent in activities of daily living Range of motion (flexion, medial rotation, lateral rotation) Pain Muscle strength (flexion, abduction, lateral rotation) Complications: haematoma, cellulitis, deep sepsis, early shoulder stiffness Mortality
Notes	

Risk of bias

Stableforth 1984 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details: "assigned by pre-arranged random selection"
Allocation concealment (selection bias)	Unclear risk	No details: "assigned by pre-arranged random selection"
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	Not blinded
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	No blinding but may not have affected appraisal of mortality
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	High risk	Large loss to follow-up (46/85 = 54%). Numbers given for those available at follow-up but incompletely reported data: only medians
Incomplete outcome data (attrition bias) Death, reoperation	Unclear risk	Slight discrepancy in trial report that 2 deaths are reported, one in each group, but long term denominators are as at baseline
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge this, but the protracted nature of this trial makes selective reporting more likely
Balance in baseline characteristics?	Unclear risk	Surgical group on average 4.5 years younger, but uncertainties mainly reflect Inadequate information in terms of other co-morbidities and injuries for this broad category of patients
Free from performance bias?	Unclear risk	Inadequate information on care programme comparability especially given the protracted nature of the trial recruitment. However, one surgeon operated throughout

Torrens 2012

Methods	Method of randomisation: use of independently produced computer-generated random numbers list Assessor blinding: no mention Loss to follow-up: 3 (1 death)
Participants	Castelldefels, Barcelona, Spain Period of study recruitment: not known 42 patients with displaced or non-displaced proximal humeral fractures that were not considered for surgery or patient refused surgery. (Included: 8 non-displaced fractures, 11 2-part and 23 3-part fractures.) Written informed consent Exclusion criteria: incapacity to understand or complete the tests or sign informed consent form; no contact of humeral head and humeral shaft, fracture dislocation, posterior displacement of the greater tuberosity ≥ 1.5 cm 32 female, 10 male; mean age 70 years, range 60 to 80 years
Interventions	Interventions started: probably very soon after patients attended with their fracture 1. Functional one week immobilisation regimen using arm sling in internal rotation 2. Conventional four weeks immobilisation regimen, using arm sling in internal rotation Both groups followed the same progressive rehabilitation programme Assigned: 20/22 Completed (at 1 year): 19/20
Outcomes	Length of follow-up: 1 year (also 1 week, and 3 and 6 months) Pain (VAS: 0 to 10: higher scores = worse pain) Constant shoulder functional score Satisfaction score (VAS: 0 to 10: higher scores = greater satisfaction) Euroqol-5D Mortality Secondary surgery and complications Further 'significant' displacement
Notes	Conference abstract (2012) presented data for 42 patients (mean age 70 years), 32 of whom had displaced fractures. A query on publication status was sent 23 May 2015, with response from Carlos Torrens received 25 May 2015: "Unfortunately this study was stopped because of lack of money so we just could recruit 40 patients." This included notification of an ongoing trial (Torrens) testing the same comparison. A data collection form sent to Carlos Torrens for this trial on June 5 2015 was returned completed by him on June 10 2015

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomisation was done by the Statistics that gave us a computer generated random numbers list." (email June 10 2015)
Allocation concealment (selection bias)	Unclear risk	No mention of safeguards.

Torrens 2012 (*Continued*)

Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	No mention of blinding.
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Not blinded but less likely that these outcomes would be affected
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Low risk	One lost to follow-up in each group.
Incomplete outcome data (attrition bias) Death, reoperation	Low risk	Data provided by trialist. One lost to follow-up in each group
Selective reporting (reporting bias)	Unclear risk	No protocol or trial registration
Balance in baseline characteristics?	Unclear risk	There were fewer 'non-displaced' fractures in the 1 week immobilisation group (1 versus 7). However, this was not statistically significant and the changes in the reported fracture distribution between abstract (4 2-part; 26 3-part; 10 non-displaced) and unpublished data (11 2-part; 23 3-part; 8 non-displaced) may indicate some intra- or inter-rater discrepancies in applying (if applied) the Neer classification system. Abstract reported "no differences as far as age, gender and displacement between conventional and functional groups". Insufficient information to confirm this
Free from performance bias?	Unclear risk	There is insufficient information to confirm this. However, it seems likely because both groups followed the same rehabilitation regimen

Voigt 2011

Methods	Method of randomisation: drawing balls from a bag by an independent person Assessor blinding: assessor blinding Loss to follow-up at 12 months: 8/56 (did not complete follow-up: 2 deaths, 4 drop-outs, 2 excluded because of early secondary arthroplasty)
Participants	Friederikenstift Hospital Hannover, Hannover, Germany Period of study recruitment: conducted over 18 month period (no dates) 56 patients with isolated Neer type 3- and 4-part proximal humeral fractures, aged > 60

	years Exclusion criteria: fractures older than 2 weeks, open fractures, pathological fractures, refractures, neurologic disease and patients who would be clearly non-compliant (e.g. alcoholics, patients of no fixed address) Of 48: 38 female, 10 male; Of 56: mean age 74 years, range 60 to 87 years
Interventions	Interventions started: at surgical fixation (time to surgery from injury not given) 1) Polyaxial locked screws: Humeral Suture Plate (HSP) (Arthrex, Naples, FL) with polyaxially locked screws. Screws were blunt-ended (considered better in the prevention of glenoid erosions in case of screw perforations) 2) Non-polyaxial (monoaxial) implant: Proximal Humerus Internal Locking System (PHILOS) (Synthes, Bettlach, Switzerland) with nonpolyaxially locked screws. (Screws were pointed in the PHILOS plate.) All surgery performed under general anaesthesia using deltopectoral approach. Tuberosity fragments reduced with fibre wire, different approaches for head fragment depending on whether valgus or varus. Allocated plate positioned anatomically and fixed with a shaft screw Patients' shoulders were immobilised in a sling for 2 days. Then, active-assisted motion beyond 90 degrees flexion and abduction were initiated avoiding the provocation of pain. At 7 weeks, free range of motion was allowed Assigned: 25/31 Completed: 20/28 (at 12 months)
Outcomes	Length of follow-up: 12 months Simple shoulder test Disability of the Arm, Shoulder and Hand (DASH) score Constant score (relative to contralateral limb) Death Complications Re-operation Range of active shoulder motion (flexion, abduction, internal rotation, external rotation) Fracture healing - AP and axillary radiographs Duration of operation Fluoroscopy time
Notes	Additional information and clarification of 8 participants who did not complete follow-up and gender data for those who completed follow-up obtained from Dr Voigt (May 2012)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"The randomization technique was blinded by drawing balls from a bag: one ball for HSP and the other ball for PHILOS by an independent person."

Voigt 2011 (*Continued*)

Allocation concealment (selection bias)	Low risk	"The randomization technique was blinded by drawing balls from a bag: one ball for HSP and the other ball for PHILOS by an independent person."
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	No mention of blinding of patients or personnel other than assessor blinding: "Follow-up evaluations postoperatively were performed in a standardized fashion by an independent trauma surgeon"
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Unlikely to influence this.
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	Although clarification on loss to follow-up (8 patients: 5 versus 3) received from author, the impact on the results for functional outcomes is unclear
Incomplete outcome data (attrition bias) Death, reoperation	Low risk	Clarification received from author on the loss to follow-up: 2 were deaths and 2 were replacement arthroplasty
Selective reporting (reporting bias)	Unclear risk	No protocol provided
Balance in baseline characteristics?	Unclear risk	Balance in 3- versus 4-part fractures, probably age and pre-operative DASH. Incomplete data on gender, 2 versus 6 with diabetes (but no frozen shoulder)
Free from performance bias?	Unclear risk	No details of surgeon experience.

Wirbel 1999

Methods	Method of randomisation: unknown, "random allocation" Assessor blinding: unlikely Loss to follow-up at 6 months: 13/77; also 14 months (9 to 36 months): 18/77
Participants	University Hospital, Homburg/Saar, Germany Period of study recruitment: January 1995 to March 1998 77 patients with displaced (separation exceeds 1 cm; fragment angulation > 30 degrees, or when tuberosity fragment is separated by > 3 mm) subcapital humeral fractures of type A1, A3, B and C1 (modified AO classification) treated by closed reduction and percutaneous fixation. Exclusion criteria: Extensive local skin infection. Impacted fractures of type A2 (treated non-surgically). Not fit enough to undergo anaesthesia and X-ray of affected shoulder

	in anterior-posterior plane. Closed reduction not feasible. 54 female, 23 male; mean age 63 years, range 6 to 89 years
Interventions	Interventions started post-operatively after percutaneous fixation (Kirschner wires plus in 38 cases, cannulated screws). 1. 1 week immobilisation in Gilchrist sling 2. 3 weeks immobilisation in Gilchrist sling Active mobilisation of elbow from first post-operative day. Active and passive physiotherapy of the shoulder (optional continuous passive motion) after removal of sling. Removal of Kirschner wires after 4 to 6 weeks, with post-procedure continuation of active exercises. Assigned: 38/39 Completed (at 6 months): 32/32
Outcomes	Length of follow-up: 9 to 36 (mean 14 months) months (in 59 participants), but also assessed at 1, 3 and 6 months Neer score Complications: avascular necrosis, local infection/haematoma, premature removal of Kirschner wires, screw removal due to subacromial impingement
Notes	Short report (1997) from conference proceedings gave interim results for 51 patients. Full report and some results provided by Dr Wirbel (February 2003). Most of the results given in the trial report were either for the whole study population or split by basic AO fracture type

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No details: "a random allocation of patients in 2 groups was done"
Allocation concealment (selection bias)	Unclear risk	No details: "a random allocation of patients in 2 groups was done"
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	No mention of blinding.
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	Not blinded but less likely that these outcomes would be affected
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	High risk	Limited data on function using a non-validated assessment instrument with a moderate loss to follow-up at 6 months (13/77 = 17%)

Wirbel 1999 (*Continued*)

Incomplete outcome data (attrition bias) Death, reoperation	Unclear risk	Incomplete data. Although loss to follow-up reported, reoperations were not sufficiently reported by treatment group
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge this.
Balance in baseline characteristics?	Low risk	No indication of any major baseline imbalance.
Free from performance bias?	Low risk	No indication of performance bias from differences in care programmes

Zhang 2011

Methods	Method of randomisation: computer generated random numbers Assessor blinding: likely, "independent" assessor at follow-up Loss to follow-up: 4 patients within the first year after surgery due to moving out of the area and change of telephone number
Participants	The Third Affiliated Hospital of Whenzou, Whenzou, China Period of study recruitment: October 2007 to September 2008 72 patients aged over 18 years with an acute closed 2-, 3- or 4-part fracture (Neer classification) of the proximal humerus treated with open reduction and internal fixation using a locking plate Exclusion criteria: pathological fractures, primary or metastatic tumour and fracture with non-union Of 68 followed-up: 46 female, 22 male; mean age 63 years, range 32 to 78 years
Interventions	Interventions started: both at surgery, time from injury not stated 1. ORIF with PHILOS locking plates (Synthes, Switzerland). Standard deltopectoral approach; reduction enabled with a K-wire under fluoroscopy. Locking plate was placed 10 mm posterior to the intertubercular groove and 10 mm distal to the tip of greater tubercle. A cortical screw was inserted initially to fix the distal fragment. Four or five locking screws were used for the fixation of the proximal fragment. All proximal screws were inserted 5 mm below subchondral bone. One or two additional locking screws were inserted obliquely into the medio-inferior region of the humeral head in this group The tubercular fragments and rotator cuff tendon were fixed using Ethibond sutures. Autograft bone was used in comminuted fractures where there was a mass defect and for reconstruction of the medial support structures. Fracture reduction and screw length were finally assessed with fluoroscopy 2. As above without medial support locking screws. All patients received prophylactic intravenous antibiotics before the procedure. Passive abduction and clock-wise rotation exercises were allowed on the day after surgery. Active rehabilitation was started six weeks postoperatively Assigned: 32/40 (total: 72) Completed (2+ years): 29/39

Zhang 2011 (*Continued*)

Outcomes	Length of follow-up: average 30.8 months (also 4, 8, 12 weeks, 6, 9 and 12 months and yearly) Shoulder function (Constant shoulder score) Union Complications: osteonecrosis of the humeral head, early failure and loss of fixation Re-operation
Notes	Personal contact (email 14/05/2012) clarified method of randomisation, group of patients who were lost to follow-up; and complications

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"The patients were randomized into two groups for study according to computer-generated random numbers" (Group sizes, however, were unequal.)
Allocation concealment (selection bias)	Unclear risk	There were insufficient safeguards (selection according to odd and even random numbers) to confirm allocation concealment
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	It is possible that the participants did not know which group they were in. The difference between the two interventions was not large. "Complications, shoulder function and radiological measurement were recorded by an independent junior doctor (YJH) who did not participate in the surgery."
Blinding (performance bias and detection bias) Death, reoperation	Low risk	These outcomes are fairly robust regarding blinding.
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	Active surveillance but missing data for 4 participants lost to follow-up. Personal correspondence gave details on complications
Incomplete outcome data (attrition bias) Death, reoperation	Unclear risk	Missing data for 4 participants. Personal correspondence provided information on re-operations
Selective reporting (reporting bias)	Unclear risk	Insufficient data to judge this. No protocol available.

Zhang 2011 (*Continued*)

Balance in baseline characteristics?	Unclear risk	Although the baseline characteristics of 68 participants were comparable, data were missing for 4 participants loss to follow-up
Free from performance bias?	Low risk	"Operations were performed by two senior surgeons." All participants received same rehabilitation

Zhu 2011

Methods	Method of randomisation: computer-generated random numbers list reviewed by nurse before surgery Assessor blinding: no, but mention of independent observer Loss to follow-up at 3 years: 6/57 (5 lost; 1 died)
Participants	Beijing Ji Shui Tan Hospital, Beijing, China Period of study recruitment: November 2004 to December 2006 57 skeletally mature patients with an acute 2-part surgical neck fracture of the proximal humerus (Neer's classification) treated surgically within 21 days of the injury. Patient consent. Exclusion criteria: open physes, fracture and displacement involving the greater or lesser tuberosity or extension of the fracture line distally beyond the deltoid tubercle, associated musculoskeletal injuries to the same upper extremity, open fracture, and prior surgery on the affected shoulder. Of 51 followed up: 34 female, 17 male; mean age 53 years
Interventions	Interventions started: surgery on average 9 days after injury (randomisation before surgery) 1. Open reduction with internal fixation using a locking plate: Locking Proximal Humeral Plate (LPHP; Synthes) or the Proximal Humeral Internal Locking System (PHILOS; Synthes). General anaesthesia combined with an interscalene block. Indirect reduction under image intensifier, with reduced fracture temporarily fixed by a Kirschner wire. After placement, position of the locking plate checked with the image intensifier intraoperatively, and the plate was fixed with locking screws. Finally, a thorough fluoroscopic screening was done to ensure that no screw was penetrating the articular surface of the humeral head 2. Open reduction with internal fixation using a locking nail: the Proximal Humeral Nail (PHN; Synthes). An interscalene brachial plexus block was used. Nail was inserted under image control without reaming after the fracture was fully reduced. After insertion of the spiral blade and the distal locking screws, an end cap was screwed in to lock the spiral blade. The rotator cuff tendon and the deltoid were carefully repaired during wound closure The affected extremity was protected by a sling for six weeks postoperatively. Passive range-of-motion exercises, supervised by a physical therapist, were initiated on the first postoperative day. Active and active-assisted exercises began after six weeks, when early callus formation could be seen on radiographs. Strengthening exercises were started three months after the surgery. Assigned: 29/28

	Completed (at 3 years): 26/25
Outcomes	Length of follow up: 3 years (also 1 year) ASES (American Shoulder and Elbow Surgeons) score Constant shoulder score (both shoulders) Pain (VAS) Mortality Complications (overall, infection (none), heterotopic ossification, screw penetration, pseudothorax) Re-operation Range of motion (active flexion, external rotation, internal rotation) Strength Duration of surgery Blood loss and transfusion Radiographic outcomes including avascular necrosis, union, and degenerative change (osteoarthritis)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Randomization was accomplished with use of a random numbers list generated by software and kept by the operating room nurse."
Allocation concealment (selection bias)	Unclear risk	"Before the surgery, the circulating nurse reviewed the random-numbers list. Patients who had been assigned an odd number were subsequently treated with a locking nail, and those who had been assigned an even number were managed with a locking plate."
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	No mention of blinding. However: "All of the follow-up physical examinations and radiographic evaluations were done by the same independent observer."
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	No mention of blinding. Lack of blinding less likely to affect these outcomes
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Low risk	Participant flow diagram provided; similar and modest losses in each group

Zhu 2011 (*Continued*)

Incomplete outcome data (attrition bias) Death, reoperation	Low risk	Participant flow diagram provided; similar and modest losses in each group: data reported
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge this.
Balance in baseline characteristics?	Unclear risk	No indication of any major baseline imbalance in 51 participants followed up at 3 years but no data for 6 participants lost to follow-up
Free from performance bias?	Low risk	All surgical procedures performed by senior surgeon and comparable rehabilitation. Although general anaesthesia used only for the plate group, this was considered unlikely to affect the findings.

Zyto 1997

Methods	Method of randomisation: sealed envelopes Independent assessor at final follow-up Loss to follow-up at 3 years: 14/43 (8 deaths, 2 could not be traced, 1 hemi-prosthesis, 3 exclusions)
Participants	Huddinge University Hospital, Stockholm, Sweden Period of study recruitment: April 1990 to February 1993 43 "elderly" patients with proximal humeral fractures (AO classification system: A 8; B 27; C 8) - see notes. In trial report: 40 patients with displaced 3- or 4-part fractures (Neer). Exclusion criteria: pathological fracture, high energy trauma, < 30% contact between humeral head and shaft, other fractures, impaired ability of patient to co-operate, relevant concomitant disease 35 female, 5 male; mean age 74 years
Interventions	Interventions started: surgery within 48 hours. 1. Internal fixation (cerclage wiring (8): or surgical tension band (14)) under general anaesthesia. Antibiotic therapy. Physiotherapy. 2. non-surgical treatment: sling for 7 to 10 days. Then physiotherapy. Assigned: 22/21; (20/20) Completed (50 months): 15/14
Outcomes	Length of follow-up: 3 to 5 years (listed as 50 months in trial report; patient questionnaire, clinical and radiological assessment); also after treatment and at 1 year: Subjective assessment of function including ability to carry 5 kg, sleep on injured side, comb hair, perform personal hygiene Constant score: overall shoulder function and components (pain, power, range of motion, activities of daily living)

	Complications: deep infection, non-union, pulmonary embolism, avascular necrosis of humeral head Mortality
Notes	Both groups had the same physiotherapy regimen. Three patients excluded from 1995 data set (Tornkvist 1995) as, on review by Zyto and a radiologist, the patients did not have 3- or 4-part fractures (personal communication) Zyto's response to a letter from H. A. Karladani admits that there may have been some inaccuracy in their classification of the fracture patterns but stressed that the Neer classification system was flawed and that other factors such as osteoporotic bone need to be considered too

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomised by sealed envelopes"
Allocation concealment (selection bias)	Unclear risk	"randomised by sealed envelopes" (at time of admission) No indication of safeguards
Blinding (performance bias and detection bias) Functional outcomes, pain, clinical outcomes, complications	High risk	Some independent assessment by radiographer and potentially by main author but no blinding
Blinding (performance bias and detection bias) Death, reoperation	Unclear risk	No blinding but may not have affected appraisal of mortality (which was not split by treatment group)
Incomplete outcome data (attrition bias) Functional outcomes, pain, clinical outcomes, complications	Unclear risk	Post-randomisation exclusions and moderately large loss to follow-up (14/43 = 32%; (11/40 = 28%))
Incomplete outcome data (attrition bias) Death, reoperation	High risk	Only whole group data presented for deaths out of 40 participants
Selective reporting (reporting bias)	High risk	Insufficient information to judge this but some post-randomisation exclusions and final follow-up performed by first author who does not appear in the earlier reports of the trial
Balance in baseline characteristics?	Low risk	No important imbalances in baseline characteristics.

Free from performance bias?	Low risk	No indications of serious performance bias: surgery performed by orthopaedic specialists who were experienced in the surgical technique

AO = Arbeitsgemeinschaft fur Osteosynthesefragen / Association for the Study of Internal Fixation (or ASIF)
AVN = avascular necrosis
A&E = accident and emergency
MI = myocardial infarction
ORIF = open reduction and internal fixation
PE = pulmonary embolism

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Bing 2002	This was a randomised clinical trial (sealed envelopes - computer-generated sequence - held in a box), recruitment 03/11/1997 to 14/01/1999, that compared Rush pins fixation with Polaris nail fixation of displaced two-part fractures of the proximal humerus. Contact with a Dr Sharma in July 2000 revealed 65 of the 80 patients in the trial had reached 2-year follow-up. Abstract by Bing et al published in 2002 indicated 40 patients of whom 30 had been followed-up for one year. Information gained via Alison Armstrong from Grahame Taylor (one of the authors of the Bing abstract) indicated that there were some concerns about the extent of missing data. Both groups had a high reoperation rate to remove metalware causing impingement. This trial has been excluded because of insufficient data It seems very likely, based on location and study dates, that the trial registration (Der Tavitian 2006) formerly awaiting classification is for this trial.
Bolano 1995	No proximal humeral fractures in a randomised trial of humeral shaft fracture treatment
Brownson 2001	This is listed in the National Research Register as a multicentre randomised trial of the management of displaced surgical neck and displaced shaft fractures of the humerus with the Halder humeral nail. Contact with Mr Brownson revealed this to be part of the trial run from Nottingham (see Wallace 2000) which had been abandoned. Mr Brownson indicated that the very specific inclusion criteria (2-part fractures with over 50% displacement) had reduced the potential sample size; patient consent had also been a problem
Carbone 2012	This is a prospective comparison of MIROS (Minimally Invasive Reduction and Osteosynthesis System®) versus traditional percutaneous pinning, each intervention being carried out at one of two hospitals in the same town in Italy. Not randomised
Chapman 1997	No proximal humeral fractures in a randomised trial of humeral shaft fracture treatment
Chiu 1997	No proximal humeral fractures in a quasi-randomised trial of humeral shaft fracture treatment

(*Continued*)

Cigni 2012	This study published only as a conference abstract compared two approaches for plate fixation. The abstract did not mention how the 40 patients "were divided in two groups", but we judged it was very unlikely this was through randomisation
De Boer 2003	This is a multicentre comparative study of locked internal fixators and non-operative treatment. Not randomised
Dias 2001	Trial abandoned. This randomised trial (random number sheets that are remotely administered) compared hemiarthroplasty versus fixation (generally suture reinforced with wires) versus non-surgical treatment (manipulation, sling for 2 weeks, then mobilisation) for 3- and 4-part fractures of the proximal humerus. Trial started in 2001, with one year follow-up (outcome was assessed by independent physiotherapists). Aimed for 90 to 100 participants, aged > 45 years. Contact with Alison Armstrong revealed that recruitment stalled at 11 patients (16 refusals) in 2008; centre stopped trial when it became a trial site for the ProFHER trial
Edelson 2008	Article mentions an abandoned randomised trial comparing "operative versus conservative care" which was unsuccessful "because patients insisted on proactively choosing rather than being assigned to a treatment group by lot"." No other details given
Elidrissi 2013	Prospective study involving 26 patients with proximal humeral fractures treated open reduction and internal fixation using an anatomical humeral plate (12 patients) or a palm tree pinning technique of Kapandji (14 patients). Inspection of the full text confirmed this was not a randomised or quasi-randomised trial
Erdoğan 2014	This study compared locking plate fixation with or without and inferomedial screw (IMS) in 36 proximal humerus fractures. Inspection of the full text showed this to be a retrospective comparison
Fan 2012	Translation of this study comparing surgical versus non-surgical treatment showed this was a retrospective comparison: "To this end, we retrospectively analyzed 2009 1 Month - January 2011 35 cases"
Flannery 2006	This is listed in the National Research Register as a randomised trial comparing non-surgical treatment and hemiarthroplasty for four-part fractures of the proximal humerus. Contact with Mr Flannery revealed his centre failed to recruit anyone into the trial. Mr Turner, the lead investigator of the multicentre trial, involving the South Thames Shoulder and Elbow Group, confirmed that the trial was abandoned due to the inability to recruit patients
Gradl 2009	Prospective study involving 152 patients with unilateral displaced and unstable proximal humeral fractures treated either with an antegrade angular and sliding stable proximal interlocking nail or an angular stable plate. Not a randomised or quasi-randomised trial
Hems 2000	This is listed in the National Research Register as a randomised trial comparing non-surgical treatment and the Halder humeral nail for displaced fractures of the surgical neck and shaft of the humerus. Contact with Mr Hems revealed this to be part of the trial run from Nottingham (see Wallace 2000) . Mr Hems indicated that they had had considerable difficulty in recruiting patients (only those with proximal humeral fractures were eligible in his centre) and had no results
IRCT2013052313435N1	The trial registration document for this study stated that it was randomised. However, a search identified a journal publication that described "prospective clinical trial, observational - Cohort studying" and

(*Continued*)

	gave no mention of random allocation. Hence this is not a randomised trial
Liao 2009	While the English abstract claims that "70 senile patients" were "randomly divided into three groups to receive different surgical methods" the distribution and characteristics (age and fracture type) of the patients in the three groups indicated serious selection bias and implied this was not a randomised trial. For example: "21 patients in the group A receiving Kirschner tension band or screw internal fixation, 37 patients in group B receiving internal fixation of locking proximal humeral plate, and 12 patients in group C receiving humeral head replacement." There was no reply to request for clarification from the lead author
Maniscalco 2014a	This was stated in the title and text of the conference abstract to be a "randomized controlled clinical trial" that compared early rehabilitation with standard rehabilitation after intramedullary nailing with a Diphos nail. However, the two groups were not concurrent and it seems that this was retrospective comparison with an historic control group. A subsequent publication of a cohort study of the nail used in this study makes no mention of this trial and adds support to our interpretation (Maniscalco 2014b).
Martetschlager 2012	The choice of intervention (deltopectoral versus anterolateral-splitting approach for locking plate fixation) was according to surgeon's preference and not "random" as suggested by the study authors. The Discussion referred to "several limitations, including its retrospective study design" of this "current study". Hence this was not a randomised or quasi-randomised controlled trial
Martin 2000	Contact with a trialist revealed that due to the discovery of problems with randomisation it was decided not to proceed with publication as the trial results could be compromised
Mechlenburg 2009	This was originally registered as a randomised controlled trial comparing a plate with a hemiarthroplasty. However, it is now registered as a prospective study of fixation with a PHILOS plate. Inger Mechlenburg confirmed that no patients had been included in the trial - the trial was abandoned because no funding was obtained
NCT00384852	The primary aim of this multicentre randomised trial was to "assess whether fracture union is accelerated in subjects with humeral fractures (proximal, diaphyseal) treated non-surgically (standard of care) and a single dose of rhBMP-2/CPM [recombinant human bone morphogenetic protein-2 (rhBMP-2)/ Calcium Phosphate Matrix] compared to subjects who receive standard of care alone". Its results were reported in a systematic review (ref 69* in Lo 2012). This reported that "While promising, the published results from the Phase II studies for humeral and femoral fractures showed little enhancement over traditional treatments [69,70]. A positive risk/benefit ratio for these treatments was not demonstrated leading to Pfizer no longer pursuing the clinical development of rhBMP-2/CPM for these applications. " Attempts over several months to obtain the report using the citation provided always met with the claim of 'server maintenance'. Unfortunately, Kevin Lo also could not supply a copy of this article (12/ 02/2015) and hence the reason for exclusion *A Phase 2, Multicenter, Double-blind, Randomized, Stratified, Controlled, Efficacy, Safety and Feasibility Study of Recombinant Human Bone Morphogenetic Protein-2 (rhBMP-2)/Calcium Phosphate Matrix (CPM) as an Adjuvant Therapy in Closed Fractures of the Humerus, Pfizer, Inc. Sep 15. 2011 ClinicalStudyResults.org,. http://www.clinicalstudyresults.org/documents/company-study_11378_0.pdf
NCT01532076	This randomised trial, which compared adipose tissue-derived mesenchymal stem cells composite graft augmentation versus acellular composite graft augmentation was terminated early after recruiting only 8 of the planned 290 participants with an isolated proximal humeral fracture

(*Continued*)

NCT02122315	The registration document indicates this completed randomised efficacy trial evaluated dry needling in post-operative shoulder pain in a mixed population of people who had proximal humeral fractures fixed with a Philos plate or people who had undergone surgical repair of a rotator cuff tear. Twenty patients were [to be] enrolled between February to April 2013. Primary outcome measure was the Constant-Murley score before and one week after the intervention (which was applied once with physical therapy) . Excluded as a mixed population and very short term follow-up
NTR2186	The registration document of this study, which compared the DePuy Delta Xtend reversed shoulder prosthesis with non-surgical treatment in the management of 4-part fractures of the proximal humerus, indicates this is not a randomised trial. The non-surgical treatment arm was a historical control group
Parnes 2005	There has been no response from the lead author of this 'trial' (last contact attempted 8 June 2012), which appears to have been reported in a conference abstract only. In 2003, 50 patients with 3- and 4-part fractures and fracture dislocations of the proximal humerus were "random selected" for surgery (closed or open reduction and external fixation or hemiarthroplasty) or non-surgical treatment. The very limited results are split descriptively according to three groups (2 reflecting the 2 different surgical methods). There is currently insufficient evidence to support this being a randomised trial
Pullen 2007	This is listed in the National Research Register Archive as a randomised trial comparing the T2 proximal humeral nail with the PHILOS plate system in patients with 2- or 3-part proximal humeral fractures. the recruitment target was 100 patients (between 01/09/2005 to 01/09/2007), and follow-up was 16 weeks. We have not located any other report of this study than the details provided in the National Research Register (UK) by, at that time, a Trauma and Orthopaedic Registrar who has now moved to another hospital. There was no response to a request for further information sent 8/6/2012. There is no indication that this study, which may not have started, will ever be reported
Rodriguez-Merchan 95	No proximal humeral fractures in a quasi-randomised trial of humeral shaft fracture treatment
Shah 2003	This is listed in the National Research Register Archive as a multicentre randomised trial of the management of four part fractures of proximal humerus that compared hemiarthroplasty versus non-surgical treatment. The recruitment target was 200 patients, with a one year follow-up using the Constant-Murley shoulder score and Oxford Shoulder score. The listed start and end dates were 01/01/2003 and 01/02/2005. No details were received of the other centres in the very limited further information received from Mr Shah in April 2003. There was no response to a request for further information sent 13/11/06. There is no indication that this study, which may not have started, will ever be reported
Sinopidis 2010	This was registered as a randomised study of reverse shoulder prosthesis and hemiarthroplasty for elderly patients with proximal humeral fractures. However, the principal investigator left the hospital (and country) before it started and a contact at Liverpool (Matthew Smith) confirmed that the study was closed after this
Wallace 2000	This is listed in the National Research Register as a multicentre randomised trial of the management of displaced surgical neck and displaced shaft fractures of the humerus with the Halder humeral nail. Contact with Prof Wallace's secretary revealed that the study had not gone ahead. The secretary mentioned three other sites (Halifax; Liverpool; and one in Scotland). No reason given. See Brownson 2001.
Wan 2005	This is a mixed population trial evaluating additional mobilisation therapy that included other fractures (e.g. clavicular and scapular fractures) as well as proximal humeral fractures. This trial was excluded

(*Continued*)

	because separate proximal humeral fracture data were not reported and the contact author is unavailable
Warnecke 1999	A multicentre prospective study but not a randomised trial.
Welsh 2000	This is listed in the National Research Register as a randomised comparison of operative and non-operative management of proximal humeral fractures. This trial was abandoned due to poor recruitment, mainly due to lack of patient consent
Yang 2006	Correspondence with the author revealed that this was not a randomised trial. The choice of surgery was dependent on the success of closed reduction
Zhang 2010	While the English abstract claims that "58 patients with 3 parts and 4 parts fractures of proximal humerus were randomly treated with AO locked compressive plates (LCP) or humeral head replacement. " the characteristics (fracture type) of the patients in the two groups indicated serious selection bias and implied this was not a randomised trial. Thus, 25 of 28 patients in the plate group had 3-part fractures (1 with a dislocation) and 3 had 4-part fractures (1 with dislocation) whereas 11 of 30 in the replacement group had 3-part fractures (2 with dislocation), 16 with 4-part fractures (4 with dislocation) and the other three had humeral head split fractures. There was no reply to request for clarification from the lead author
Zuckerman 2012	Commentary only on Olerud 2011b.

Characteristics of studies awaiting assessment *[ordered by study ID]*

Battistella 2011

Methods	"Randomized clinical study"
Participants	54 patients (38 female, 26 male, mean age 61 years) with 2-part surgical neck fractures or 3-part valgus impacted fractures
Interventions	Surgery involving a titanium plate: 1. Minimally invasive fixation based on anterolateral deltoid split approach and percutaneous reduction 2. Open reduction and internal fixation by standard deltopectoral approach
Outcomes	Constant score, instrumental activities of daily living, pain (VAS), range of motion, union, complications
Notes	Requests for further information sent to Dr Battistella (8 and 14 May 2012) were unsuccessful

Brorson 2009

Methods	Multicentre, randomised clinical trial (central randomisation unit)
Participants	25 recruited out of a planned 162 patients with displaced 4-part fractures of the proximal humerus

Brorson 2009 (*Continued*)

Interventions	1. Hemiarthroplasty 2. Fixed-angle plate osteosynthesis 3. Non-surgical treatment
Outcomes	Follow-up: 3 years (primary outcome: 1 year) Primary outcome: Constant Disability Scale Secondary outcomes: Oxford Shoulder Score, Short Form-36
Notes	• Published protocol. • Correspondence from Stig Brorson (June 11 2012) reveals a slower than anticipated recruitment. (Start date: April 2009; End date: March 2013 (final date for primary outcome measure)) • Entry for trial (clinicaltrials.gov) on January 19 2015, indicated that "The recruitment status of this study is unknown because the information has not been verified recently". Status as "recruiting" had been last verified on June 2012 by Herlev Hospital. The study completion date had been changed from March 2012 to March 2013. • Correspondence from Stig Brorson (January 28 2015) revealed: "Unfortunately, we had to stop inclusion after 25 patients. They all followed the protocol and were evaluated accordingly. However, 9 out of 11 centres withdrew from the study because they found allocation of patients with 4-part fractures to non-surgical treatment ethically problematic. Ironically, we are now unable to continue the study as most surgeons find plating of 4-part fractures problematic! All data on the 25 patients are available." Stig Brorson further clarified (February 6 2015): "We enrolled 25 patients and randomly allocated them to non-surgical treatment, ORIF with locking plate or HA. Two died before the first evaluation, no drop-outs. The remaining 23 patients were evaluated after 12 months with blinded and non-blinded Constant Score, Oxford Shoulder Score and Short-Form 36. All data are available and unpublished." • Trial transferred from Ongoing to Studies awaiting classification (11/02/2015) Discussions are taking place on the most suitable approach to take with this data set (23/05/2015)

Liu 2011

Methods	"Randomly divided"
Participants	50 patients aged 60 or above with proximal humeral fractures Mean 70 years (range 60 to 83 years); 36 female, 14 male; 19 two-part, 21 three-part and 10 four-part fractures
Interventions	1. PHILOS plate augmentation with minimally invasive injectable graft (MIIG) X3 Hivisc 2. PHILOS plate alone Minimally invasive percutaneous plate osteosynthesis used in both groups
Outcomes	Follow-up: mean 18 months (range 12 to 25 months) Neer scoring system, complications, healing time, operative time, blood loss
Notes	No response to inquiry on method of allocation sent 07/12/14; baseline imbalance in type of fracture with more 3-part and 4-part fractures in the first group

Luo 2008

Methods	Patients were randomly allocated via a random numbers table.
Participants	60 patients (32 females, 28 males; age range: 39 to 62 years) treated operatively for fracture of the surgical neck of the humerus
Interventions	1. Acupuncture (electroacupuncture and infrared radiation) plus passive exercise of the shoulder joint 2. Exercises only: passive exercise of the shoulder joint followed by active exercises Treatment lasted 1 month.
Outcomes	Follow-up: 1 month Shoulder pain score (VAS) Shoulder joint activity
Notes	Trial in Chinese with English abstract. Translation of methods section (1.1) confirmed that this was a randomised trial

NCT02052206

Methods	Randomised trial
Participants	80 patients with either osteoarthritis of the shoulder or complex proximal humeral fractures
Interventions	For shoulder replacement surgery 1. computer assisted 3D planning 2. conventional 2D planning.
Outcomes	Follow-up: 6 weeks and 1 year Primary outcome: Discrepancy (difference of translation in mm and rotation in degrees) in the realised position of the components compared with the preoperative planning (CT scans) Secondary outcomes: Clinical outcome, subjective shoulder value, Constant score
Notes	Study not open to recruitment (January 2014); but is now open to recruitment (May 2015) Contact: Lazaros Vlachopoulos, Balgrist University Hospital, Switzerland

Wang 2013

Methods	"Randomly divided"
Participants	80 "elderly" patients with proximal humerus fractures Mean 67 years (range 60 to 83 years); 42 female, 38 male; AO classification: 12 A, 45 B and 23 C fractures
Interventions	1. Minimally invasive percutaneous insertion of PHILOS plate with injectable bone 2. Minimally invasive percutaneous insertion of PHILOS plate alone
Outcomes	Length of follow-up: unknown Constant score, complications, healing time, bone mineral density, patient satisfaction with results of treatment

Wang 2013 (*Continued*)

Notes	No response to inquiry on method of allocation sent 15/01/14; translated title from Chinese states this is a "case-control" study. Data extracted from abstract. (Unusually high Constant score in the bone substitute group: 97.2 (SD 4.6)). Translation required if considered study should be included in future

Zhu 2014

Methods	patients "randomly either underwent"
Participants	40 people with comminuted proximal humeral fractures (however, "patients with evidence of arthrosis or a clinical follow-up shorter than 12 months were excluded")
Interventions	1. Locking plate and an autologous crest bone graft 2. Locking plate only
Outcomes	Length of follow-up: mean 25 months, range 13 to 48 months Range of motion, pain, SF-36, return to previous activities or occupation, complications, time to union was also recorded.
Notes	Queries on allocation method and donor site complications/morbidity sent 22 May 2015

Characteristics of ongoing studies *[ordered by study ID]*

ACTRN12610000730000

Trial name or title	Minimally invasive versus standard open reduction of proximal humerus fractures Official title: A prospective randomised controlled trial comparing clinical and radiographic outcomes of the deltopectoral and limited deltoid splitting approaches for fixation of displaced proximal humeral fractures in a skeletally mature population
Methods	Single-centre, randomised controlled trial. Computer generated random list. Unblinded
Participants	90 patients with displaced proximal humeral fractures
Interventions	1. Minimally invasive approach with closed reduction and temporary fixation with k-wires, then the limited deltoid splitting approach (locking plate) 2. Standard open reduction and internal fixation via the deltopectoral approach (locking plate)
Outcomes	Follow-up: 1 year Primary outcome: Constant Shoulder Score and DASH (Disabilities of the Arm, Shoulder, and Hand) Score Secondary outcomes: radiographic outcomes, complications, union rate
Starting date	Anticipated start date: October 2010 (however, study is not yet recruiting)
Contact information	Jeremy Stanley 14 Grand Drive Remuera

ACTRN12610000730000 (*Continued*)

	Auckland 1050 New Zealand jellystan@hotmail.com
Notes	Trial was not recruiting (nor ethics approval) at time of registration (02/09/2010) No change on checking February 11 2015

DELPHI

Trial name or title	Clinical investigation for fractures of the proximal humerus in elderly patients. A randomized study of two surgical treatments: Reverse total shoulder arthroplasty versus angular stable device Philos
Methods	Randomised trial; 6 centres "semi-blinded" for the physiotherapist who will examine the patients
Participants	120 patients, aged 65 years to 85 years, admitted in hospital with a displaced three- or four-part proximal humerus fracture of OTA/AO group 11-B2 or 11-C2 (displaced fracture of extra-articular or articular, bifocal type)
Interventions	1. Reversed shoulder prosthesis 2. ORIF with PHILOS plate
Outcomes	Follow-up: 3, 6, 12 and 24 months, and five years Primary outcome: Constant score Secondary outcomes: Oxford Shoulder score; quality of life measured with the 15D score, health economics, radiographic results
Starting date	Start date: January 2013 Estimated completion date: June 2021 (June 2021 = final data collection date for primary outcome measure)
Contact information	Dr Tore Fjalestad Orthopaedic Department, Division of surgery and Clinical Neuroscience Oslo University Hospital HF Nydalen, Postbox 4950 Oslo, Norway torfja@online.no
Notes	This appeared in Studies awaiting assessment in 2012 version of the review as Fjalestad (RCT proposal) Published protocol available Recruiting status verified in October 2014 by Oslo University Hospital

HOMERUS

Trial name or title	Hemiarthroplasty versus osteosynthesis in humeral fractures (HOMERUS): A multicentre randomised trial Official title: Three- and four-part fracture of the proximal humerus in the elderly. Angle stable locking compression plate osteosynthesis versus hemiarthroplasty
Methods	Multicentre, randomised clinical trial. Single blinded (outcomes assessor)
Participants	134 patients aged over 60 years with displaced 3- and 4-part proximal humeral fractures with more than 5 mm of dislocation in one of the fracture planes
Interventions	1. Hemiarthroplasty 2. Angle stable locking compression plate osteosynthesis
Outcomes	Follow-up: 2 years Primary outcome: DASH (Disabilities of the Arm, Shoulder, and Hand) score Secondary outcomes: VAS (Visual analogue score) for pain and patient satisfaction, Constant-Murley Score, SF-36, Radiographic evaluation, complications
Starting date	Start date: September 2010 Anticipated completion date: August 2012
Contact information	Dr PA Verbeek Department of Orthopaedic Surgery University Medical Centre Groningen (UMCG) Groningen The Netherlands paulverbeek@gmail.com
Notes	

HURA

Trial name or title	A randomised clinical trial comparing a lateral minimally invasive approach and the traditional anterior approach for plating of proximal humerus fractures
Methods	Randomised, single blind (outcome assessors), clinical trial
Participants	90 patients, with humeral surgical neck fracture, Neer II valgus-type, and Neer III
Interventions	1. Lateral minimally invasive approach (plate fixation) 2. Deltopectoral approach (plate fixation)
Outcomes	Follow-up: 3, 6, and 12 weeks, and at 6, 12, 18 and 24 months Primary outcome: Quick DASH Secondary outcomes: SF-12v2 Questionnaire, Constant Shoulder Score, the Patient Scar Assessment Scale, complication rate
Starting date	Start date: November 2007 End date: January 2018 (January 2016 = final data collection date for primary outcome)

HURA (*Continued*)

Contact information	Marie-France Poirer Hopital Sacré-Coeur Montreal Quebec Canada H4J1C5 mariefrancepoirier@hotmail.com
Notes	Entry for trial (clinicaltrials.gov) on April 10 2012, indicated that "The recruitment status of this study is unknown because the information has not been verified recently" Entry for trial (clinicaltrials.gov) on January 19 2015, indicated that "This study is currently recruiting participants"; "Verified August 2014 by Université de Montreal" End date of study changed from January 2012 to January 2018

NCT00438633

Trial name or title	Early vs delayed physical therapy (exercises) for non-operatively-treated proximal humerus fractures: a prospective randomized trial
Methods	Randomised trial
Participants	60 patients, aged 18 years or over, with non-operatively treated proximal humeral fractures
Interventions	1. Physical therapy started immediately after diagnosis of injury 2. Physical therapy delayed until 3 weeks after diagnosis of injury
Outcomes	Follow-up: 6 months Primary outcome: shoulder flexion Secondary outcomes: shoulder pain Likert scores; external and internal rotation; abduction; DASH and Constant scores
Starting date	Start date: February 2005 End date: December 2013 (December 2012 = final data collection date for primary outcome measure)
Contact information	Prof David Ring Director of Research Hand Service Massachusetts General Hospital Boston Massachusetts USA dring@partners.org
Notes	Changes to NCT00438633 on 27 May 2008 seemed to indicate that, despite its official title, this is now a prospective cohort study (accessed: April 10 2012). David Ring confirmed it was still an RCT (April 16 2012) Entry for trial (clinicaltrials.gov) on January 19 2015, indicated that "This study is enrolling participants by invitation only", last verified July 2012. The study design was still listed as a prospective cohort

NCT00818987

Trial name or title	A multicentre prospective randomized control trial on the treatment of three- and four-part proximal humerus fractures in patients 70 years and older: comparing open reduction and internal fixation with non operative treatment
Methods	Randomised controlled trial: "randomly (like flipping a coin)"
Participants	120 patients aged 70 years or over with a 3- or 4-part fracture
Interventions	1. Open reduction and internal fixation 2. Non-operative treatment (reduction and immobilisation)
Outcomes	Follow-up: 1 year Primary outcome: patients' functional shoulder scores as measured by the Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire Secondary outcomes: functional and mental status instruments (i.e. SF-36/EQ-5D) used to assess the patient's health-related quality of life; re-operation rates; and the time required to return to pre-injury level of independence
Starting date	November 2010 Estimated completion date: October 2011
Contact information	Contact: Raman Johal (raman.johal@vch.ca) Principal investigator: Pierre Guy, University of British Columbia, Canada
Notes	As of registration update (17/02/2011) the study was recruiting. Start and end dates amended. Entry for trial (clinicaltrials.gov) on January 19 2015, indicated that "The recruitment status of this study is unknown because the information has not been verified recently". Status as "recruiting" had been last verified on February 2011

NCT00999193

Trial name or title	Effectiveness and cost-effectiveness of operative and conservative treatment of comminuted fractures of the proximal humerus. A randomised, controlled study
Methods	Randomised single blind (outcomes assessor)
Participants	90 older patients with comminuted, displaced fractures of the proximal humerus Inclusion criteria: Age over 65 years; acute trauma with randomisation within 7 days of injury; 3- or 4-part fracture with > 5 mm dislocation of the anatomic neck (AO classification C1-2 for non-luxation fractures; C3 for luxation fractures)
Interventions	1. PHILOS locking plate: open reduction of the fracture (and GH joint), internal fixation with the PHILOS locking plate. Tuberculum fragments are sutured to the plate with thick non-absorbable suture. 2. Global FX hemiarthroplasty: replacement of the humeral articular head with hemiprosthesis. Tubercles are sutured to the prosthesis with thick nonabsorbable sutures. 3. Non-surgical treatment: immobilisation in a supporting brace for 3 weeks, then increasingly active rehabilitation programme supported by a physiotherapist until 12 weeks of the injury

NCT00999193 (*Continued*)

Outcomes	Follow-up: 24 months Primary outcomes: Pain at rest and activity (Numeric Rating Scale), Constant score Secondary outcomes: Simple Shoulder test (SST), Disabilities of the Arm, Shoulder and Hand (DASH), quality-of-life assessment (15D), subjective patient satisfaction, complications and costs
Starting date	November 2010 End date: December 2018 (December 2016 = final data collection date for primary outcome)
Contact information	Tuomas Lähdeoja, MD: tuomas.lahdeoja@hus.fi Mika Paavola, MD: mika.paavola@hus.fi Helsinki University, Helsinki, Finland
Notes	As of registration update (22/01/2012) the study was recruiting. Start and end dates amended. Entry for trial (clinicaltrials.gov) on January 19 2015, indicated that "This study is currently recruiting participants"; "Verified October 2014 by Helsinki University" Study completion date changed from November 2014 to December 2018. The estimated enrolment dropped from 150 to 90

NCT01086202

Trial name or title	Clinical outcome comparison between medial and lateral offset reverse shoulder arthroplasty
Methods	Randomised single blinded trial
Participants	40 patients aged between the ages of 50 and 95 years of age who are a candidate for a reverse shoulder arthroplasty. This includes patients with rotator cuff tear arthroplasty, irreparable rotator cuff tears, significant proximal humerus fractures and malunions, and chronic proximal humerus dislocators
Interventions	Tornier reversed shoulder arthroplasty: 1. Medial offset design 2. Lateral offset design
Outcomes	Follow-up: 2 years Shoulder functional score Pain scores Radiological outcomes
Starting date	May 2010 End date: April 2012
Contact information	Wesley Phipatanakul, MD wphip@hotmail.com Principal investigator: Montri D Wongworawat, MD, Loma Linda University Health Department of Orthopaedic Surgery, Loma Linda Californa 92354 USA

NCT01086202 (*Continued*)

Notes	The future inclusion of this mixed population trial will depend on the numbers of participants with proximal humeral fractures. As of registration update (21/06/2011) the study was still recruiting

NCT01113411

Trial name or title	Effectiveness of intensive rehabilitation on shoulder function after a fracture of the proximal humerus treated by locked plate. A prospective randomized study
Methods	Randomised clinical trial
Participants	80 patients aged over 18 years treated by PHILOS locked plate system for unstable closed fracture of the proximal humerus (two-part and three-part fractures according to the Neer classification) within 7 days on injury
Interventions	1. Early and intensive exercise programme A thoraco brachial brace will be worn for 48 hours following the surgery and then removed for the remainder of treatment. Patients will then start the intensive rehabilitation programme without physical therapy. The exercise programme will be provided to the patient. The exercises consist of active and active-assisted movements of the shoulder for a period of six weeks, limiting external rotation to 0°. Patients are encouraged to use their affected limb for daily activities. Strengthening exercises are started the 6th week following surgery and the full programme will be completed three months after surgery. Patients who wish can then continue their rehabilitation with a physiotherapist. The patient will complete a daily diary to validate the frequency and intensity of the exercises versus 2. Standard rehabilitation programme The patient will wear the thoraco brachial brace for a period of four weeks following the surgery. It may be taken off for hygiene purposes and dressing. After the four weeks, the patient will take the brace off permanently and begin an exercise programme, writing down the frequency and intensity of the exercises. Physiotherapy is allowed for the remaining part of the three months rehabilitation programme
Outcomes	Length of follow-up: 12 months Primary outcome: Constant score (adjusted for age) at 6 months. A difference of 10 points is considered significant (standard deviation of 15 points). Secondary outcomes: reoperation, redisplacement, Constant score at 12 months, Dash, return to professional activities, pain, range of motion
Starting date	December 2009 Final follow-up date: December 2013 (final data collection date for primary outcome)
Contact information	Hélène Côté, Reg. Nurse: helco3@hotmail.com Stéphane Pelet, MD, PhD: spelet01@hotmail.com Hopital de l'Enfant-Jésus, Canada
Notes	Entry for trial (clinicaltrials.gov) on January 19 2015, indicated that "The recruitment status of this study is unknown because the information has not been verified recently". Status as "recruiting" had been last verified on December 2012. The study completion date had been changed from December 2012 to December 2013

NCT01524965

Trial name or title	The effect of the timing of postoperative mobilisation after locking plate osteosynthesis of fractures of the surgical neck of the humerus
Methods	Randomised controlled trial Single blind (outcomes assessor)
Participants	100 patients, 18 years or older, with surgery performed within 10 days of injury for a dislocated (> 1 cm or 35 degrees) AO 11-A2, -A3, -B1 or -B2 fracture of the surgical neck of the proximal humerus with a possible fracture of the greater tuberosity
Interventions	1. Immediate mobilisation after open reduction and Philos plate fixation: immediate passive range of motion exercises are begun postoperatively, after 3 weeks, active unloaded mobilisation begins after three weeks and active, loaded use is allowed 6 weeks postoperatively 2. Standard mobilisation after open reduction and Philos plate fixation: immediately postoperatively the arm is held in a sling, active mobilisation of healthy joints and pendulum exercises are begun. Passive range of motion exercises of the shoulder are begun 3 weeks postoperatively. Active mobilisation begins after six weeks
Outcomes	Follow-up: 3 and 6 weeks, 3, 6, 12 and 24 months Primary outcome: DASH (Disabilities of the Arm, Shoulder, and Hand) score Secondary outcomes: Constant score, simple shoulder test (SST), pain at rest and during motion, subjective satisfaction, quality of life using the 15D instrument, complications
Starting date	May 2011 Estimated completed date: December 2016 (December 2016 = final data collection date for primary outcome)
Contact information	Tuomas Lahdeoja, MD Töölö Hospital, Helsinki University Central Hospital Helsinki, Finland, 00029 tuomas.lahdeoja@hus.fi
Notes	Verified as recruiting participants in October 2014 by Helsinki University

NCT01557413

Trial name or title	Randomised study between intramedullary locking nails and locking plates for treatment of proximal humerus fractures (HUMERUS) Official title: Randomised study between intramedullary locking nails and locking plates for treatment of proximal humerus fractures in patients after 40-year-old
Methods	Single centre, randomised controlled trial. Unblinded.
Participants	84 patients, aged between 40 and 85 years, with a type III or IV "cephalotuberosity" proximal humeral fracture (classification of Neer and DUPARC)
Interventions	1. Intramedullary nail (Multilock, Synthes) 2. Locking plate (SURFIX, Integra)

NCT01557413 (*Continued*)

Outcomes	Follow-up: 1 year Primary outcome: Constant Score Secondary outcomes: Quick DASH, complication (malunion, necrosis, infection)
Starting date	Start date: February 2012 Estimated completion date: February 2017 (final data collection for primary outcome)
Contact information	Dr Patrick Boyer Group Hospitalier Bichat - Claude Bernard 46, rue Henri-Huchard Paris Ile de France France 75018 patrick.boyer@bch.aphp.fr
Notes	Entry for trial (clinicaltrials.gov) on January 19 2015, indicated that "This study is currently recruiting participants"; "Verified August 2014 by Assistance Publique - Hôpitaux de Paris". Study completion date changed from November 2015 to February 2017. The estimated enrolment dropped from 144 to 84

NCT01847508

Trial name or title	A multicenter randomized controlled trial to investigate the treatment outcome of PHILOS screw augmentation compared to PHILOS without augmentation in older adult patients with proximal humerus fractures
Methods	Randomised controlled trial
Participants	128 (planned enrolment) patients aged 65 years or older with an acute ($\leq$ 10 days) closed fracture of the proximal humerus after low energy trauma. Any displaced or unstable 3- or 4-part fracture of the proximal humerus (i.e. segment displacement > 0.5 cm or angulated > 45°) except isolated displaced fractures of the greater or lesser tuberosity Exclusion criteria: bilateral or previous proximal humerus fractures on either side, splitting fracture of the humeral head or humeral head impression fracture, cuff-arthropathy of the contra- or ipsilateral proximal humerus, associated nerve or vessel injury, any known clotting disorders, severe cardiac and/or pulmonary insufficiency, known hypersensitivity or allergy to any of the components of Traumacem V+ Cement Kit, any severe systemic disease (class 4 - 6 of the American Society of Anesthesiologists (ASA) physical status classification), any not-medically-managed severe systemic disease (class 3 of the ASA physical status classification), recent history of substance abuse, prisoner
Interventions	1. PHILOS screw augmentation: Proximal Humeral Internal Locking System with screw tip augmentation (PHILOS+) with high viscous polymethylmethacrylate (PMMA) cement (Traumacem V+) 2. Proximal Humeral Internal Locking System (PHILOS)
Outcomes	Follow-up: 1 year (primary outcome) Primary outcome: Any occurrence of radiographically confirmed mechanical failure during the first year after treatment Secondary outcomes include: quality of life, intra- and postoperative adverse events related to the procedure and/or device, reoperation rate, surgical details including of augmentation, shoulder function (Shoulder Pain and Disability Index (SPADI), shoulder function (Constant score, shoulder function (Disabilities of the Arm, Shoulder and Hand Score (QuickDASH))

NCT01847508 (*Continued*)

Starting date	October 2013 Final follow-up date: September 2016 (final data collection date for primary outcome measure)
Contact information	Jan Ljungqvist, +41 44 200 24 61 jan.ljungqvist@aofoundation.org
Notes	Recruiting confirmed January 2015

NCT01984112

Trial name or title	Proximal humerus fractures: randomized study between intramedullary locking nails and locking plates for Neer 2- and 3-part displaced fractures
Methods	Randomised controlled trial
Participants	72 patients, aged 50 years to 85 years, with acute closed fractures (less than 21 days since injury) of the proximal humerus classified as 2- or 3-parts of Neer, with involvement of the humeral head and one of the tuberosities
Interventions	1. Intramedullary locked nail performed by antero-lateral transdeltoid minimally invasive approach and rotator cuff augmentation with non-absorbable polyester suture 2. Osteosynthesis with Philos plate, through deltopectoral approach and rotator cuff augmentation with non-absorbable polyester suture
Outcomes	Follow-up: 12 months Primary outcome: absolute Constant-Murley score Secondary outcomes: DASH (Disability of Arm-Shoulder-Hand) score, UCLA (University of California Los Angeles) score, individual relative Constant-Murley score compared with non-injured shoulder, overall complications and need for additional surgery, post-operative integrity of the rotator cuff evaluated by ultrasonography
Starting date	May 2011 Final follow-up date: December 2015 (final data collection date for primary outcome)
Contact information	Mauro Gracitelli, MD Instituto de Ortopedia e Traumatologia São Paulo, SP, Brazil, 05403-010 mgracitelli@gmail.com
Notes	Verified in November 2013 as recruiting participants by University of Sao Paulo

NCT02075476

Trial name or title	Prospective, randomized and double blind study of parallel groups for evaluating the effectiveness between two surgical techniques for reconstruction of humeral proximal extremity fractures or fractures luxation in three or four fragments of Neer's classification
Methods	Randomised controlled trial
Participants	40 patients, aged 70 years or over, with "humeral proximal extremity fracture or fracture luxation in three or four fragments of Neer's classification"
Interventions	1. Reverse arthroplasty Delta Xtent (DePuy) 2. Hemiarthroplasty Global Fx (DePuy)
Outcomes	Follow-up: 1, 3, 6, 12, 18 and 24 months Primary outcome: ASES (American Shoulder and Elbow) score Secondary outcomes: intra-operative complications; post-operative complications, surgical time, recovery time
Starting date	May 2013 Estimated completed date: May 2016 (May 2015 = final data collection date for primary outcome)
Contact information	Carlos Alvarez, MD Hospital General Universitario Gregorio Marañon Madrid, Spain, 28007 calvargon@gmail.com
Notes	Verified as recruiting participants in March 2014 by Hospital General Universitario Gregorio Marañon

NTR3208

Trial name or title	Arthroplasty in three- and four-part proximal humerus fracture: hemi or reverse? Prospective multicentre randomised clinical trial
Methods	Multicentre, randomised controlled trial. Unblinded.
Participants	52 patients aged over 65 years with displaced 3- or 4-part proximal humerus fractures who are candidates for primary shoulder arthroplasty
Interventions	1. Aequalis reverse fracture prosthesis 2. Aequalis fracture prosthesis
Outcomes	Follow-up: 1 year Primary outcome: Constant Shoulder Score Secondary outcomes: DASH (Disabilities of the Arm, Shoulder, and Hand) Score, SF-12 questionnaire, Visual Analogue Score of pain
Starting date	Start date: July 2010 Estimated completion date: December 2014

NTR3208 (*Continued*)

Contact information	Yde Engelsma Medisch Centrum Alkmaar Wilhelminalaan 12 1815 JD Alkmaar The Netherlands y.engelsma@mca.nl
Notes	

NTR4019

Trial name or title	PROMOTION-trial: A PROspective randomized Multicenter trial for the treatment of dislocated 3-part proximal humerus fractures: Open reduction and internal fixaTION versus intramedullary nailing
Methods	Randomised controlled trial
Participants	92 patients, aged 18 years or over, with unilateral displaced 3-part proximal humeral fracture (> 45 degrees or > 0.5 cm displacement between major fracture fragments)
Interventions	1. Philos plate (Proximal humeral internal locking system, Synthes) 2. PHN (Proximal Humeral Nailing system, Stryker)
Outcomes	Follow-up: 1 year Primary outcome: Constant-Murley score Secondary outcomes: DASH-score, pain, SF-12, EQ-5D, complication and mortality rate
Starting date	1 August 2013 Planned closing date: 31 July 2017
Contact information	Jeroen Bransen Maastrict University Medical Centre Department of Surgery PO Box 5800 6202 AZ Maastricht The Netherlands jeroenbransen@gmail.com
Notes	Ethics approval not received for this multicentre trial at time of registration (3 June 2013)

ProCon

Trial name or title	Primary hemiarthroplasty versus conservative treatment for comminuted fractures of the proximal humerus in the elderly (ProCon) - a multicenter randomized trial
Methods	Randomised trial: “variable block randomisation will be accomplished via a trial website”

ProCon (*Continued*)

Participants	Patients (65 years or older) with a comminuted proximal humeral fracture 80 patients (65 years or older) with a comminuted proximal humeral fracture: three-part (Hertel classification type 9, 10, 11), four-part (Hertel type 12), anatomical neck (Hertel type 2), or split-head fractures of the humeral head
Interventions	1. Hemiarthroplasty (Affinis® Fracture shoulder endoprosthesis) 2. Non-surgical treatment (collar and cuff for three weeks)
Outcomes	Follow-up: 1, 3 and 6 weeks, and 3, 6, 12 and 24 months Primary outcome (Constant Score) and secondary outcomes (DASH, pain, radiographic healing, secondary intervention rates, complication rates, mortality rates, SF-36, and EQ-5D) Costs for (in)formal healthcare consumption
Starting date	Start date: 15 June 2009 Planned end date: 31 December 2013
Contact information	Dennis Den Hartog Department of Surgery-Traumatology Erasmus MC University Medical Center Rotterdam P.O. Box 2040 3000 CA Rotterdam The Netherlands d.denhartog@erasmusmc.nl
Notes	Published protocol

ROTATE

Trial name or title	Return Of funcTion And exTErnal rotation post proximal humerus fracture fixation with neutral rotation brace (ROTATE)
Methods	Randomised controlled trial
Participants	100 patients (planned), aged over 18 years, with proximal humeral fractures requiring operative intervention with extramedullary plate fixation (i.e. fractures displaced by 1 cm and/or angulated by 45 degrees or more
Interventions	Post-surgery sling 1. External rotation of the shoulder in a neutral rotation brace 2. Polysling holding the proximal humerus in internal rotation The operation, post-operative treatment and planned physiotherapy will be the same in the two groups
Outcomes	Follow-up: 6 weeks, 9 weeks, 3 months and 1 year Primary outcomes: Oxford shoulder score (1 year), DASH (the Disabilities of the Arm, Shoulder and Hand) (1 year) Secondary outcomes: range of movement (flexion, extension, abduction, external and internal rotation), SF-12 score, time to union of fracture, return to work post surgery, re-operations and complications

ROTATE (*Continued*)

Starting date	Start date: January 2013 End date: December 2015
Contact information	Ms Victoria Conboy, FRCS (Orth) (Principal Investigator) Consultant in Trauma and Orthopaedics Torbay District General Hospital Lawes Bridge Torquay TQ2 7AA United Kingdom veronica.conboy@nhs.net
Notes	Sponsor: South Devon Healthcare NHS Foundation Trust

SHeRPA

Trial name or title	Comparison of two shoulder replacement methods after trauma
Methods	Multicentre (5 centres in the UK), randomised controlled trial. Participants are blinded
Participants	50 patients aged over 65 years with displaced 3- or 4-part proximal humerus fractures; fit for surgery Exclusion: dementia, non consent, unfit for reverse shoulder arthroplasty, glenoid fracture, axillary nerve palsy
Interventions	1. Reverse total shoulder arthroplasty 2. Hemiarthroplasty
Outcomes	Follow-up: 2 years, also 6 weeks, 3 and 12 months Primary outcome: Constant Shoulder Score (at 12 months) Secondary outcomes: QuickDASH (Disabilities of the Arm, Shoulder, and Hand) Score, Oxford Shoulder Score, ASES score
Starting date	Start date: June 2013 Estimated completion date: August 2017
Contact information	Adam Watts Wrightington Hospital Hall Lane Appley Bridge Wigan Lancashire WN6 9EP United Kingdom
Notes	Retrospectively registered (applied: 13/01/2015) after end of recruitment Funder: Tornier UK Limited (probably manufacturer of implants under test)

Torrens

Trial name or title	Management of conservatively treated proximal humeral fractures: prospective randomized study (taken from Torrens 2012a)
Methods	Randomised controlled trial (use of computer-generated random numbers)
Participants	80 participants with non-surgically treated proximal humeral fractures
Interventions	1. Functional one week immobilisation regimen 2. Conventional four weeks immobilisation regimen Both groups will follow the same progressive rehabilitation programme
Outcomes	Length of follow-up: 1 year (also 1 week, and 3 and 6 months) Pain (analogue pain scale: EVA), Constant shoulder functional score, satisfaction score, Euroqol-5D, secondary surgery (based on Torrens 2012a)
Starting date	Late 2012 (May 25 2015: "started 6 months ago")
Contact information	Carlos Torrens, MD, Castelldefels, Spain Email: CTorrens@parcdesalutmar.cat
Notes	In response to a query on the status of Torrens 2012a, Carlos Torrens (25 May 2015): "Unfortunately this study was stopped because of lack of money so we just could recruit 40 patients. Right now we have found money again and we re-started it 6 months ago, so I hope that during this year we will be able to recruit 80 patients and we will follow them 1 year meaning that in 2 years we will be able to publish more consistent results." Confirmation received from Carlos Torrens on June 4 2015 that this is a new trial

TPHF

Trial name or title	Treatment of Proximal Humeral Fractures (TPHF) Official title: A national, prospective, randomized, multicenter, controlled head-to-head comparison of conservative, plate fixation and prosthesis in treatment of displaced 2-, 3- and 4 part fractures of proximal humerus of 60 years and older patients
Methods	Multicentre, randomised clinical trial. Single blinded (outcomes assessor)
Participants	290 patients aged over 60 years with displaced 2-, 3- and 4-part proximal humeral fractures
Interventions	1. PHILOS locking plate 2. Epoca prosthesis 3. Non-surgical management
Outcomes	Follow-up: 2 years Primary outcome: DASH (Disabilities of the Arm, Shoulder, and Hand) score Secondary outcome: EQ-5D Questionnaire

TPHF (*Continued*)

Starting date	Start date: January 2011 Estimated completion date: September 2018 (December 2016 = final data collection date for primary outcome)
Contact information	Antti Launonen Tampere University Hospital Tampere Pirkanmaa Finland, 33521 antti.launonen@pshp.fi
Notes	As of registration update (01/02/2011), trial was recruiting in Tampere University Hospital, but recruitment had not started in Oulu or Kuopio Entry for trial (clinicaltrials.gov) on January 19 2015, indicated that "This study is currently recruiting participants"; "Verified November 2014 by Tampere University Hospital". End date of study changed from September 2016 to September 2018

AO = Arbeitsgemeinschaft fur Osteosynthesefragen / Association for the Study of Internal Fixation (or ASIF)
LCP = Locking compression plate
NRR = National Research Register
ORIF = open reduction and internal fixation

DATA AND ANALYSES

Comparison 1. Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Shoulder disability: Croft Shoulder Disability Score	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Disability (1 or more problems) at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Severe disability (5 or more problems) at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 Disability (1 or more problems) at 2 years	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.4 Severe disability (5 or more problems) at 2 years	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Croft shoulder disability score: individual problems at 2 years	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.1 Pain on movement	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 Bathing difficulties	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 Change position at night more often	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.4 Disturbed sleep	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.5 No active pastimes or usual physical recreation	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.6 Lifting problems	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.7 Help needed	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.8 More accidents (e.g. dropping things)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Number of treatment sessions (until independent function achieved)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4 SF-36 scores: pain & physical dimensions	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 Physical functioning (0-100: excellent) at 16 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 Physical functioning (0-100: excellent) at 1 year	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 Role limitation physical (0-100: none) at 16 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.4 Role limitation physical (0-100: none) at 1 year	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.5 Pain (0-100: none) at 16 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.6 Pain (0-100: none) at 1 year	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

5 Quality of life assessment: EuroQol 5D (0: dead to 1: best health)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.1 At 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.2 At 6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.3 At 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Adverse events	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Frozen shoulder	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.01, 7.95]
6.2 Fracture displacement	2	106	Risk Ratio (M-H, Fixed, 95% CI)	2.2 [0.22, 22.45]
6.3 Non-union	2	106	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.4 Complex regional pain syndrome type 1	2	115	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.07, 16.71]
6.5 Treated (injection) subacromial impingement	1	64	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.07, 15.30]
6.6 Shoulder complications	4	259	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.15, 3.63]
6.7 Fracture complications	2	106	Risk Ratio (M-H, Fixed, 95% CI)	2.2 [0.22, 22.45]
7 Mortality	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8 Constant shoulder score (ratio of affected/unaffected arm)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.1 8 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 16 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.3 1 year	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Constant shoulder score (0 to 100: best)	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
9.1 At 6 weeks	1	64	Mean Difference (IV, Fixed, 95% CI)	10.10 [2.02, 18.18]
9.2 At 3 months	2	106	Mean Difference (IV, Fixed, 95% CI)	6.53 [0.77, 12.30]
9.3 At 6 months	2	105	Mean Difference (IV, Fixed, 95% CI)	3.39 [-1.46, 8.24]
9.4 At 12 months	1	39	Mean Difference (IV, Fixed, 95% CI)	1.46 [-7.05, 9.97]
9.5 6 months: subjective assessment (0 to 35: best)	1	64	Mean Difference (IV, Fixed, 95% CI)	1.90 [-0.54, 4.34]
9.6 6 months: objective assessment range of motion and strength (0 to 65: best)	1	64	Mean Difference (IV, Fixed, 95% CI)	4.10 [-0.62, 8.82]
10 Pain VAS (0 to 100: worst pain)	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.1 At 6 weeks	1	64	Mean Difference (IV, Fixed, 95% CI)	-3.60 [-20.76, 13.56]
10.2 At 3 months	2	106	Mean Difference (IV, Fixed, 95% CI)	-5.13 [-14.76, 4.50]
10.3 At 6 months	2	105	Mean Difference (IV, Fixed, 95% CI)	4.29 [-5.48, 14.07]
10.4 At 12 months	1	39	Mean Difference (IV, Fixed, 95% CI)	10.8 [-4.59, 26.19]
11 Changes in pain intensity (mm) from baseline: 100 mm visual analogue scale (positive change = less pain)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
11.1 At 6 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.2 At 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.3 At 6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Range of motion at 6 months (degrees): difference between two shoulders	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
12.1 Abduction	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.2 Anterior elevation	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.3 Lateral rotation	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

13 Patient dissatisfied with treatment	1	Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
14 Patient satisfaction (0 to 10: higher scores - greater satisfaction)	1	Mean Difference (IV, Fixed, 95% CI)	Totals not selected
14.1 At 3 months	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.2 At 6 months	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.3 At 12 months	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 2. Gilchrist bandage versus 'Classic' Desault bandage

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Problems with bandages	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Application of bandage was uncomfortable	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Premature bandage removal	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Fracture displacement by 3 weeks	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3 Poor or bad rating by patient at fracture consolidation	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Comparison 3. Instructed self-exercise versus conventional physiotherapy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain at one year (scale 0 to 8: maximum pain)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Severe or moderate pain at 3 months	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3 Requested change of therapy	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
4 Adverse events (frozen shoulder: 1 v 2; unexplained prolonged pain: 0 v 1)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
5 Neer's rating (0 to 100: best) at mean 16 months (exploratory analysis)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6 Active gleno-humeral elevation (degrees)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 4. Surgical versus non-surgical treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Functional scores at 12 months (higher = better outcome)	5	419	Std. Mean Difference (IV, Fixed, 95% CI)	0.07 [-0.12, 0.26]
1.1 DASH (0 to 100: worst disability) (reversed)	2	105	Std. Mean Difference (IV, Fixed, 95% CI)	0.19 [-0.19, 0.57]
1.2 ASES (0 to 24: best)	1	48	Std. Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.67, 0.46]
1.3 SST (0 to 12: best)	1	47	Std. Mean Difference (IV, Fixed, 95% CI)	0.11 [-0.46, 0.69]
1.4 OSS (0 to 48: best)	1	219	Std. Mean Difference (IV, Fixed, 95% CI)	0.04 [-0.22, 0.31]
2 Functional scores at 24 months (higher = better outcome)	4	351	Std. Mean Difference (IV, Fixed, 95% CI)	0.07 [-0.14, 0.28]
2.1 DASH (0 to 100: worst disability) (reversed)	2	99	Std. Mean Difference (IV, Fixed, 95% CI)	0.33 [-0.07, 0.73]
2.2 ASES (0 to 24: best)	1	42	Std. Mean Difference (IV, Fixed, 95% CI)	-0.02 [-0.62, 0.59]
2.3 OSS (0 to 48: best)	1	210	Std. Mean Difference (IV, Fixed, 95% CI)	-0.03 [-0.30, 0.24]
3 Oxford Shoulder Score (0 to 48: best outcome)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.1 Over 2 years	1	231	Mean Difference (IV, Fixed, 95% CI)	0.75 [-1.68, 3.18]
3.2 At 6 months	1	226	Mean Difference (IV, Fixed, 95% CI)	2.25 [-0.42, 4.92]
3.3 At 12 months	1	219	Mean Difference (IV, Fixed, 95% CI)	0.43 [-2.10, 2.96]
3.4 At 24 months	1	210	Mean Difference (IV, Fixed, 95% CI)	-0.29 [-2.84, 2.26]
4 DASH (0 to 100: worst disability)	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.1 at 4 months	2	106	Mean Difference (IV, Fixed, 95% CI)	0.91 [-7.00, 8.83]
4.2 at 12 months	2	105	Mean Difference (IV, Fixed, 95% CI)	-4.51 [-13.50, 4.48]
4.3 at 24 months	2	99	Mean Difference (IV, Fixed, 95% CI)	-7.43 [-16.26, 1.41]
5 American Shoulder and Elbow Surgeons score (0 to 24: best)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.1 at 6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.2 at 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.3 at 24 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Simple Shoulder Test (0 to 12: best function)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 at 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Activities of daily living	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
7.1 Unable to manage personal hygiene at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 Unable to comb hair at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 Unable to sleep on fractured side at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.4 Unable to carry 5 kg at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.5 Unable to manage personal hygiene at 50 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.6 Unable to comb hair at 50 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

7.7 Unable to sleep on fractured side at 50 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.8 Unable to carry 5 kg at 50 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Quality of life assessment: EuroQol (0: dead to 1: best health)	4		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
8.1 at 3 to 4 months	4	360	Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.02, 0.04]
8.2 at 6 months	4	381	Mean Difference (IV, Fixed, 95% CI)	0.04 [0.01, 0.08]
8.3 at 12 months	4	371	Mean Difference (IV, Fixed, 95% CI)	0.02 [-0.02, 0.06]
8.4 at 24 months	4	354	Mean Difference (IV, Fixed, 95% CI)	0.03 [-0.01, 0.08]
9 Quality of life assessment (Fjalestad 2010 and 2014 data)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
9.1 15D at 3 months (0: death; 1: perfect health)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 15D at 6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 15D at 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.4 number of QALYs at 1 year	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.5 numbers of QALYs at 1 year (- deaths)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.6 15D at 24 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Quality of life: SF-12 Physical Component Score (0 to 100: best)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.1 at 6 months	1	216	Mean Difference (IV, Fixed, 95% CI)	2.60 [-0.24, 5.44]
10.2 at 12 months	1	218	Mean Difference (IV, Fixed, 95% CI)	1.5 [-1.42, 4.42]
10.3 at 24 months	1	210	Mean Difference (IV, Fixed, 95% CI)	1.10 [-1.99, 4.19]
11 Quality of life: SF-12 Mental Component Score (0 to 100: best)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
11.1 at 6 months	1	216	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-3.57, 2.37]
11.2 at 12 months	1	218	Mean Difference (IV, Fixed, 95% CI)	-2.0 [-4.81, 0.81]
11.3 at 24 months	1	210	Mean Difference (IV, Fixed, 95% CI)	-1.40 [-4.33, 1.53]
12 Mortality	6	496	Risk Ratio (M-H, Fixed, 95% CI)	1.40 [0.69, 2.83]
13 Additional surgery (re-operation or secondary surgery)	7	523	Risk Ratio (M-H, Fixed, 95% CI)	2.06 [1.18, 3.60]
13.1 at 6 to 12 months	3	113	Risk Ratio (M-H, Fixed, 95% CI)	1.37 [0.32, 5.93]
13.2 at 2 years	4	410	Risk Ratio (M-H, Fixed, 95% CI)	2.20 [1.20, 4.04]
14 Adverse events / complications	8		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
14.1 Number of patients with complications	1	250	Risk Ratio (M-H, Fixed, 95% CI)	1.30 [0.80, 2.11]
14.2 Additional shoulder-related therapy	1	250	Risk Ratio (M-H, Fixed, 95% CI)	1.75 [0.53, 5.83]
14.3 Infection	8	559	Risk Ratio (M-H, Fixed, 95% CI)	4.31 [1.11, 16.74]
14.4 Nerve injury / palsy	4	396	Risk Ratio (M-H, Fixed, 95% CI)	1.16 [0.37, 3.59]
14.5 Non-union	7	523	Risk Ratio (M-H, Fixed, 95% CI)	0.43 [0.19, 0.98]
14.6 Avascular necrosis	7	513	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.53, 1.32]
14.7 Symptomatic malunion	1	250	Risk Ratio (M-H, Fixed, 95% CI)	0.8 [0.22, 2.91]
14.8 Screw penetration into joint	3	160	Risk Ratio (M-H, Fixed, 95% CI)	11.49 [2.25, 58.76]

14.9 Metalwork (internal fixation) problems	1	250	Risk Ratio (M-H, Fixed, 95% CI)	21.0 [1.24, 354.53]
14.10 Wire penetration at 1 year	1	38	Risk Ratio (M-H, Fixed, 95% CI)	3.0 [0.13, 69.31]
14.11 Redisplacement resulting in an operation	2	81	Risk Ratio (M-H, Fixed, 95% CI)	0.26 [0.03, 2.22]
14.12 Implant-related (hemiarthroplasty) failure	2	300	Risk Ratio (M-H, Fixed, 95% CI)	4.0 [0.45, 35.18]
14.13 Secondary dislocation or resorption of the greater tuberosity	2	101	Risk Ratio (M-H, Fixed, 95% CI)	13.15 [1.78, 96.90]
14.14 Tuberosity displacement at 50 months	1	29	Risk Ratio (M-H, Fixed, 95% CI)	0.15 [0.01, 2.71]
14.15 Fixation failure resulting in an operation	1	50	Risk Ratio (M-H, Fixed, 95% CI)	3.0 [0.13, 70.30]
14.16 Refracture	1	22	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.07, 14.05]
14.17 Post-traumatic stiffness	1	250	Risk Ratio (M-H, Fixed, 95% CI)	1.2 [0.38, 3.83]
14.18 Impingement	2	308	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.18, 5.62]
14.19 Rotator cuff tear	2	300	Risk Ratio (M-H, Fixed, 95% CI)	3.0 [0.48, 18.73]
14.20 Post-traumatic stiffness	1	250	Risk Ratio (M-H, Fixed, 95% CI)	1.2 [0.38, 3.83]
14.21 CRPS or severe pain	1	250	Risk Ratio (M-H, Fixed, 95% CI)	2.0 [0.18, 21.78]
14.22 Dislocation or instability	1	250	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.01, 8.10]
14.23 Heterotopic ossification	1	50	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.24 Post-traumatic osteoarthritis (signs of)	4	183	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.27, 1.70]
15 Dependent in activities of daily living (or dead) at 6 months	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
16 Constant scores (overall: 0 to 100: best score)	5		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
16.1 at 3-4 months	3	156	Mean Difference (IV, Fixed, 95% CI)	-2.90 [-7.35, 1.56]
16.2 at 12 months	4	199	Mean Difference (IV, Fixed, 95% CI)	2.81 [-2.20, 7.82]
16.3 at 24 months	3	143	Mean Difference (IV, Fixed, 95% CI)	-0.25 [-6.75, 6.25]
16.4 at 50 months	1	29	Mean Difference (IV, Fixed, 95% CI)	-5.0 [-17.52, 7.52]
17 Constant scores (difference between injured and uninjured shoulder): Normal = 0.	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
17.1 at 6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.2 at 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.3 at 24 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Poor or unsatisfactory function at 1 year (Neer rating)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
19 VAS disability (0 to 100: no restrictions)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
19.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.2 at 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Pain: VAS (0 to 100: worst pain)	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
20.1 At 3 months	1	49	Mean Difference (IV, Fixed, 95% CI)	-18.0 [-29.03, -6.97]
20.2 At 2 years	2	101	Mean Difference (IV, Fixed, 95% CI)	-6.38 [-14.18, 1.41]

21 Constant score at 50 months: overall and components	1	Mean Difference (IV, Fixed, 95% CI)	Totals not selected
21.1 Overall score (0-100: best score)	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.2 Pain (maximum score 15)	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.3 Range of motion (maximum score 40)	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.4 Power (maximum score 25)	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.5 Activities of daily living (maximum score 20)	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Constant (often severe) pain at 6 months	1	Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
23 Failure to recover 75% muscle power relative to other arm (survivors) at 6 months	1	Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
23.1 Flexion	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.2 Abduction	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.3 Lateral rotation	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
24 Range of movement impairments in survivors at 6 months	1	Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
24.1 Flexion < 45 degrees	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
24.2 Unable to place thumb on mid spine (T12)	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
24.3 Lateral rotation < 5 degrees	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 Costs at 1 year (Euros in 2005)		Other data	No numeric data
26 Total costs including indirect costs (Euros) at 1 year	1	Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 5. Locking plate versus locking intramedullary nail

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 American Shoulder and Elbow Surgeons (ASES) score (0 to 100: best)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 At 1 year	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 At 3 years	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Death, re-operation and adverse events	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.1 Death	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 Any complication	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 Screw penetration into humeral head (all had re-operation)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

2.4 Heterotopic ossification	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.5 Infection	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.6 Osteonecrosis	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.7 Degenerative change of glenohumeral joint	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.8 Secondary varus collapse	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.9 Non-union	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Pain (VAS: 0 to 10: worst)		Other data	No numeric data
4 Constant score (0 to 100: best)	1	Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 At 1 year	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 At 3 year	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Active range of motion (at 3 years)	1	Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.1 Forward elevation (degrees)	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.2 External rotation	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Range of movement: internal rotation (level on spine)		Other data	No numeric data
7 Strength of suprapinatus (relative to opposite side) % - at 3 years	1	Mean Difference (IV, Fixed, 95% CI)	Totals not selected
7.1 At 1 year	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 At 3 years	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Operation times and blood loss	1	Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.1 Duration of surgery (minutes)	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 Blood loss (ml)	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Intra-operative complication	1	Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
9.1 Pneumothorax	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 Blood transfusion	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 6. Locking plate versus intramedullary nails (Zifko method)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complications and [slight] malunion	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Any complication	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Malunion (usually slight)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Constant score (% of healthy limb) at mean 2 years	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Time to union and time to recover upper limb function (weeks)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 Time to radiographic union	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Time to recover normal upper limb function	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

4 Operation and fluoroscopic times	1	Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 Duration of operation (minutes)	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 X-ray exposure (minutes)	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Length of hospital stay (days)	1	Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 7. Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 DASH score (0 to 100: worst disability)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 At 4 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 At 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 At 24 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 EQ-5D score (0 to 1: best quality of life)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 At 4 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 At 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 At 24 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Re-operation	2	62	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.10, 1.10]
3.1 Hemiarthroplasty versus tension band wiring	1	30	Risk Ratio (M-H, Fixed, 95% CI)	0.09 [0.01, 1.51]
3.2 Hemiarthroplasty versus locking plate fixation	1	32	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.16, 2.88]
4 Dead at 2 years	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
5 Implant removal at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6 Constant score (0 to 100: best score)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.1 At 4 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 At 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 At 24 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Pain VAS (0 to 100: worst pain) at 24 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8 Pain at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
9 Range of motion at 24 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
9.1 Flexion (degrees)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 Extension (degrees)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 8. Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Shoulder function scores at 24 to 49 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 Quick DASH score (0 to 55: worst outcome)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Re-operation	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3 Death	1	62	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Composite (objective and subjective) shoulder function scores at 24 to 49 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 UCLA score (0 to 35: best outcome)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 Constant score (0 to 100: best outcome)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 Constant % relative to opposite side	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Constant score at 24 to 49 months: overall and components	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.1 Overall score (0-100: best score)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.2 Pain (maximum score 15)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.3 Range of motion (maximum score 40)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.4 Power (maximum score 25)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.5 Activities of daily living (maximum score 20)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Complications	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6.1 Any complication	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 Intra-operative fracture	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 Deep infection	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.4 Superficial infection	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.5 Haematoma	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.6 Neurological complications	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.7 Severe stiffness	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.8 Proximal migration of implant	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Radiological assessment findings	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
7.1 Malunion of tuberosities	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 Resorption of tuberosities	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 Scapular notching	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.4 Heterotopic ossification	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Range of motion (degrees) at 24 to 49 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.1 Anterior forward	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

8.2 Abduction	1	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 9. Deltoid-split versus deltopectoral approaches for plate fixation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Re-operation	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 For complication or a fall	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Plate removal by patient request	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Dead at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3 Complications	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3.1 Injurious fall on shoulder	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Axillary nerve damage	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 Screw perforation	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.4 Implant (head or shaft) loosening	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.5 Deep infection	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.6 Humeral head necrosis	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Constant score (0 to 100: best score)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 At 6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 At 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Pain (VAS 0 to 10: intolerable pain)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.1 At 6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.2 At 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Operation and fluoroscopic times	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.1 Duration of operation (minutes)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 X-ray exposure (minutes)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Length of hospital stay (days)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 10. Polyaxial versus monoaxial screw insertion in plate fixation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 DASH score at 12 months (0 to 100: greatest disability)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Simple shoulder test (0 to 12: best outcome)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 At 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 At 6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 At 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

3 Re-operation	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 By 6 months	1	66	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.15, 4.76]
3.2 By 1 year	2	180	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.58, 2.08]
4 Dead at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
5 Constant score at 12 months (% of contralateral limb)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6 Complications (radiological assessment)	2		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6.1 Any complication	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 Primary implant malposition	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 Secondary loss of reduction and screw perforation	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.4 Non-union / delayed union due to osteonecrosis (6 months)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.5 Avascular necrosis at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.6 Varus deformity (> 10 / ≥20 degrees)	2		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.7 Greater tuberosity displacement	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.8 Screw cut-out (intra-articular)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Range of motion (degrees) at 12 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
7.1 Flexion	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 Abduction	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 External rotation	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.4 Internal rotation	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Operation and fluoroscopic times	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.1 Duration of operation (minutes)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 Fluoroscopic time (minutes)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 11. Medial support screws versus control for locking plate fixation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Adverse events	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Early loss of fixation	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Re-operation for early failure	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 Osteonecrosis (asymptomatic)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

2 Constant score (0 to 100: best) at 2.5 years	1	Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 12. MultiLoc Proximal Humeral Nail (MPHN) versus Polarus nail

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Adverse events	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Re-operation	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Post-op impingement	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 Screw loosening	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.4 Non-union	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.5 Rotator cuff symptoms	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.6 Intra-operative complications	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.7 Mortality	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.8 Radiographic malunion	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Constant score (0 to 100: best outcome) at 14 months (6 to 22 months)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Unadjusted Constant score	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 Adjusted Constant score	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Range of shoulder motion (degrees)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 Lateral elevation	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Forward flexion	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 External rotation	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Lengths of surgery and hospital stay	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 Length of surgery (minutes)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 Length of hospital stay (days)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 13. Hemiarthoplasty: EPOCA prosthesis versus HAS prosthesis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Adverse events	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Deep infection	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Persistent pain - scheduled for reoperation	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Radiological assessment findings	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.1 Resorption of tuberosities	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

2.2 Secondary dislocation of tuberosities	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 Superior migration of prosthesis	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.4 Anterior subluxations	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.5 Glenoid erosion	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.6 Aseptic loosening of stem	1	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Range of motion results at one year (degrees)		Other data	No numeric data

Comparison 14. Hemiarthroplasty: tenodesis of long head of biceps (LHB) versus LHB tendon left intact

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complications and further surgery	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Any complication	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Further surgery for listed complications	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 Deep infection	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.4 Tuberosity malunion	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.5 Inferior subluxation of prosthesis	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.6 Loss of reduction of greater tuberosity	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Constant score (0 to 100: best function) at 2 years	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Shoulder pain at 2 year follow-up	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
4 Active shoulder elevation (degrees) at 2 years	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 15. Post-operative (percutaneous fixation) immobilisation for 1 week versus 3 weeks

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Neer score $\leq$ 80 points (unsatisfactory or failure) at 6 months	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2 Premature removal of Kirschner wires	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Comparison 16. Post-operative (hemiarthroplasty) mobilisation: early (2 weeks immobilisation) versus late (6 weeks)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Oxford Shoulder Score at 1 year (adjusted: 0 to 100 best)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Constant shoulder score (at 1 year)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Overall score (0 to 100: best)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 Pain component (0 to 15: best))	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 Activities of daily living component (0 to 25: best)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.4 Mobility component (0 to 40: best)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.5 Strength component (0 to 25: best)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Radiological assessment findings	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3.1 Non-union (with bone resorption)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Malunion	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 Greater tuberosity migration (all had severe pain at 6 & 12 months)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.4 Superior luxation of prosthesis	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Range of motion at 1 year	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 Elevation (degrees)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 External rotation (degrees)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 1.1. Comparison 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks, Outcome 1 Shoulder disability: Croft Shoulder Disability Score.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks

Outcome: 1 Shoulder disability: Croft Shoulder Disability Score

Study or subgroup	Early (≤ 1 week) n/N	3 or 4 weeks n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Disability (1 or more problems) at 1 year				
Hodgson 2003	18/42	29/40		0.59 [0.40, 0.88]
2 Severe disability (5 or more problems) at 1 year				
Hodgson 2003	13/42	17/40		0.73 [0.41, 1.30]
3 Disability (1 or more problems) at 2 years				
Hodgson 2003	16/37	22/37		0.73 [0.46, 1.15]
4 Severe disability (5 or more problems) at 2 years				
Hodgson 2003	12/37	13/37		0.92 [0.49, 1.75]

Analysis 1.2. Comparison 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks, Outcome 2 Croft shoulder disability score: individual problems at 2 years.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks

Outcome: 2 Croft shoulder disability score: individual problems at 2 years

Study or subgroup	Early (≤ 1 week) n/N	3 or 4 weeks n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Pain on movement				
Hodgson 2003	5/37	13/37		0.38 [0.15, 0.97]
2 Bathing difficulties				
Hodgson 2003	4/37	7/37		0.57 [0.18, 1.79]
3 Change position at night more often				
Hodgson 2003	6/37	12/37		0.50 [0.21, 1.19]
4 Disturbed sleep				
Hodgson 2003	3/37	6/37		0.50 [0.14, 1.85]
5 No active pastimes or usual physical recreation				
Hodgson 2003	6/37	3/37		2.00 [0.54, 7.40]
6 Lifting problems				
Hodgson 2003	16/37	15/37		1.07 [0.62, 1.83]
7 Help needed				
Hodgson 2003	9/37	6/37		1.50 [0.59, 3.79]
8 More accidents (e.g. dropping things)				
Hodgson 2003	9/37	5/37		1.80 [0.67, 4.86]

Analysis 1.3. Comparison 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks, Outcome 3 Number of treatment sessions (until independent function achieved).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks

Outcome: 3 Number of treatment sessions (until independent function achieved)

Study or subgroup	Early (≤ 1 week) N	Mean(SD)	3 or 4 weeks N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Hodgson 2003	44	9 (6)	42	14 (9)		-5.00 [-8.25, -1.75]

Analysis 1.4. Comparison 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks, Outcome 4 SF-36 scores: pain & physical dimensions.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks

Outcome: 4 SF-36 scores: pain % physical dimensions

Study or subgroup	Early (≤ 1 week) N	Mean(SD)	3 or 4 weeks N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Physical functioning (0-100: excellent) at 16 weeks						
Hodgson 2003	42	69.9 (25.1)	39	69.2 (23.6)		0.70 [-9.91, 11.31]
2 Physical functioning (0-100: excellent) at 1 year						
Hodgson 2003	40	65.4 (31.3)	40	68.4 (30.2)		-3.00 [-16.48, 10.48]
3 Role limitation physical (0-100: none) at 16 weeks						
Hodgson 2003	42	61.9 (43.6)	39	39.7 (40.8)		22.20 [3.82, 40.58]
4 Role limitation physical (0-100: none) at 1 year						
Hodgson 2003	40	60 (44.1)	40	54.4 (44.2)		5.60 [-13.75, 24.95]
5 Pain (0-100: none) at 16 weeks						
Hodgson 2003	42	72 (20.6)	39	59.9 (20)		12.10 [3.26, 20.94]

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Study or subgroup	Early (≤ 1 week) N	Mean(SD)	3 or 4 weeks N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
6 Pain (0-100: none) at 1 year						
Hodgson 2003	40	69.2 (27.2)	40	65.6 (26.6)		3.60 [-8.19, 15.39]

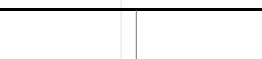
Analysis 1.5. Comparison 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks, Outcome 5 Quality of life assessment: EuroQol 5D (0: dead to 1: best health).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks

Outcome: 5 Quality of life assessment: EuroQol 5D (0: dead to 1: best health)

Study or subgroup	Early (≤ 1 week) N	Mean(SD)	3 or 4 weeks N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 At 3 months						
Torrens 2012	20	0.62 (0.22)	22	0.72 (0.19)		-0.10 [-0.22, 0.02]
2 At 6 months						
Torrens 2012	20	0.65 (0.21)	21	0.72 (0.21)		-0.07 [-0.20, 0.06]
3 At 12 months						
Torrens 2012	19	0.67 (0.2)	20	0.76 (0.19)		-0.09 [-0.21, 0.03]



Analysis 1.6. Comparison 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks, Outcome 6 Adverse events.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks

Outcome: 6 Adverse events

Study or subgroup	Early (≤ 1 week) n/N	3 or 4 weeks n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Frozen shoulder					
Hodgson 2003	0/40	1/40		100.0 %	0.33 [0.01, 7.95]
Subtotal (95% CI)	**40**	**40**		**100.0 %**	**0.33 [0.01, 7.95]**
Total events: 0 (Early (≤ 1 week)), 1 (3 or 4 weeks)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.68 (P = 0.50)					
2 Fracture displacement					
Lefevre-Colau 2007	0/32	0/32			Not estimable
Torrens 2012 (1)	2/20	1/22		100.0 %	2.20 [0.22, 22.45]
Subtotal (95% CI)	**52**	**54**		**100.0 %**	**2.20 [0.22, 22.45]**
Total events: 2 (Early (≤ 1 week)), 1 (3 or 4 weeks)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.67 (P = 0.51)					
3 Non-union					
Lefevre-Colau 2007	0/32	0/32			Not estimable
Torrens 2012	0/20	0/22			Not estimable
Subtotal (95% CI)	**52**	**54**			**Not estimable**
Total events: 0 (Early (≤ 1 week)), 0 (3 or 4 weeks)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
4 Complex regional pain syndrome type 1					
Kristiansen 1989	1/35	1/38		100.0 %	1.09 [0.07, 16.71]
Torrens 2012	0/20	0/22			Not estimable
Subtotal (95% CI)	**55**	**60**		**100.0 %**	**1.09 [0.07, 16.71]**
Total events: 1 (Early (≤ 1 week)), 1 (3 or 4 weeks)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.06 (P = 0.95)					
5 Treated (injection) subacromial impingement					
Lefevre-Colau 2007	1/32	1/32		100.0 %	1.00 [0.07, 15.30]
Subtotal (95% CI)	**32**	**32**		**100.0 %**	**1.00 [0.07, 15.30]**
Total events: 1 (Early (≤ 1 week)), 1 (3 or 4 weeks)					
Heterogeneity: not applicable					

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Study or subgroup	Early (≤ 1 week) n/N	3 or 4 weeks n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Test for overall effect: Z = 0.0 (P = 1.0)					
6 Shoulder complications					
Hodgson 2003 (2)	0/40	1/40		43.4 %	0.33 [0.01, 7.95]
Kristiansen 1989 (3)	1/35	1/38		27.7 %	1.09 [0.07, 16.71]
Lefevre-Colau 2007 (4)	1/32	1/32		28.9 %	1.00 [0.07, 15.30]
Torrens 2012 (5)	0/20	0/22			Not estimable
Subtotal (95% CI)	**127**	**132**		**100.0 %**	**0.73 [0.15, 3.63]**
Total events: 2 (Early (≤ 1 week)), 3 (3 or 4 weeks)					
Heterogeneity: Chi^2 = 0.37, df = 2 (P = 0.83); I^2 =0.0%					
Test for overall effect: Z = 0.38 (P = 0.71)					
7 Fracture complications					
Lefevre-Colau 2007 (6)	0/32	0/32			Not estimable
Torrens 2012 (7)	2/20	1/22		100.0 %	2.20 [0.22, 22.45]
Subtotal (95% CI)	**52**	**54**		**100.0 %**	**2.20 [0.22, 22.45]**
Total events: 2 (Early (≤ 1 week)), 1 (3 or 4 weeks)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.67 (P = 0.51)					

(1) None required surgery

(2) Frozen shoulder

(3) CRPS1

(4) Treated subacromial impingement

(5) CRPS1

(6) Reporting on fracture displacement and non-union

(7) All were fracture displacement (no non-union)

Analysis 1.7. Comparison 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks, Outcome 7 Mortality.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks

Outcome: 7 Mortality

Study or subgroup	Early (≤ 1 week) n/N	3 or 4 weeks n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Torrens 2012	0/20	1/22		0.37 [0.02, 8.48]

Analysis 1.8. Comparison 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks, Outcome 8 Constant shoulder score (ratio of affected/unaffected arm).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks

Outcome: 8 Constant shoulder score (ratio of affected/unaffected arm)

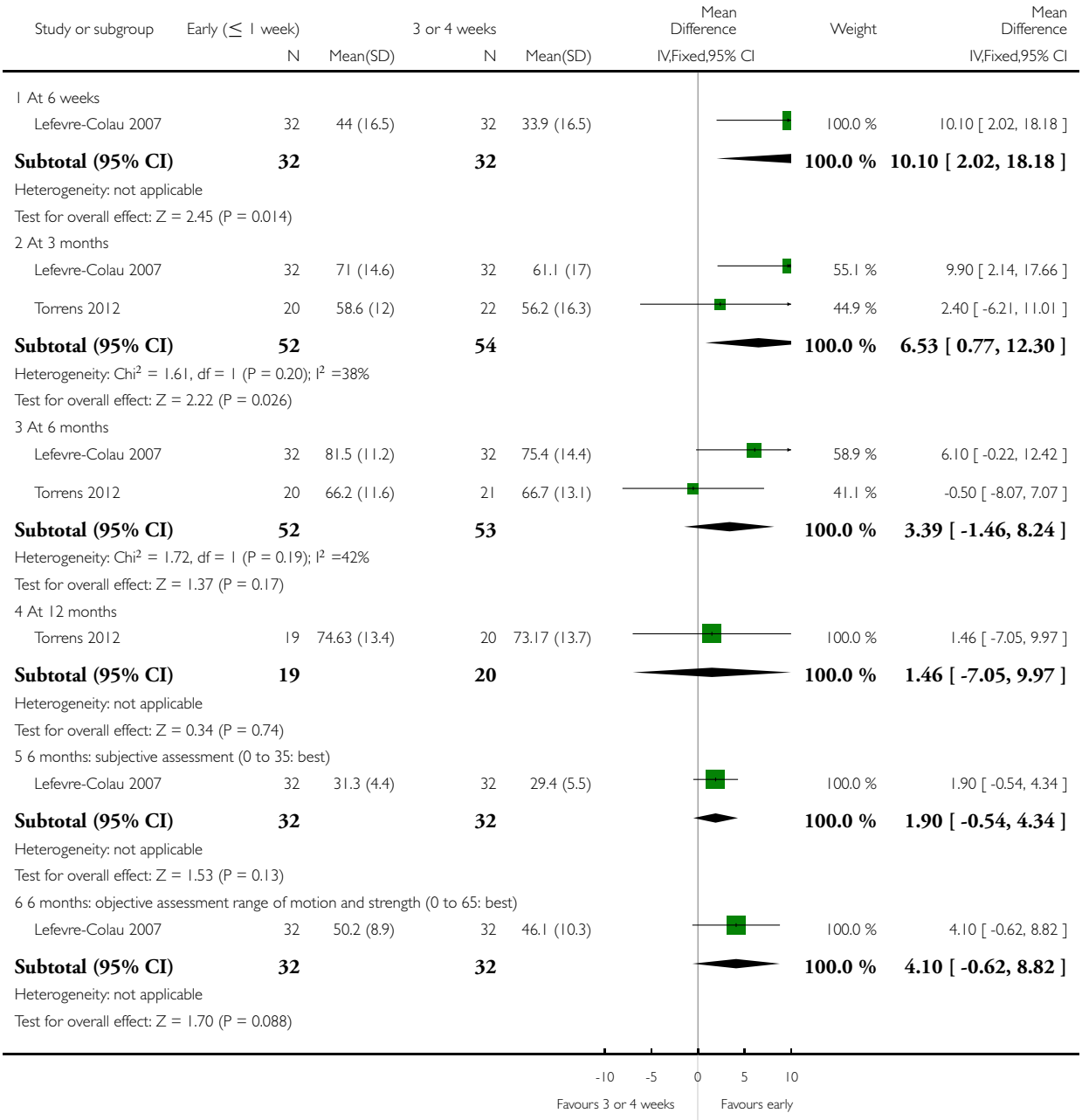
Study or subgroup	Early (≤ 1 week) N	Mean(SD)	3 or 4 weeks N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 8 weeks						
Hodgson 2003	43	0.57 (0.26)	40	0.39 (0.19)		0.18 [0.08, 0.28]
2 16 weeks						
Hodgson 2003	42	0.7 (0.21)	40	0.54 (0.2)		0.16 [0.07, 0.25]
3 1 year						
Hodgson 2003	41	0.82 (0.23)	41	0.75 (0.25)		0.07 [-0.03, 0.17]

Analysis 1.9. Comparison 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks, Outcome 9 Constant shoulder score (0 to 100: best).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks

Outcome: 9 Constant shoulder score (0 to 100: best)

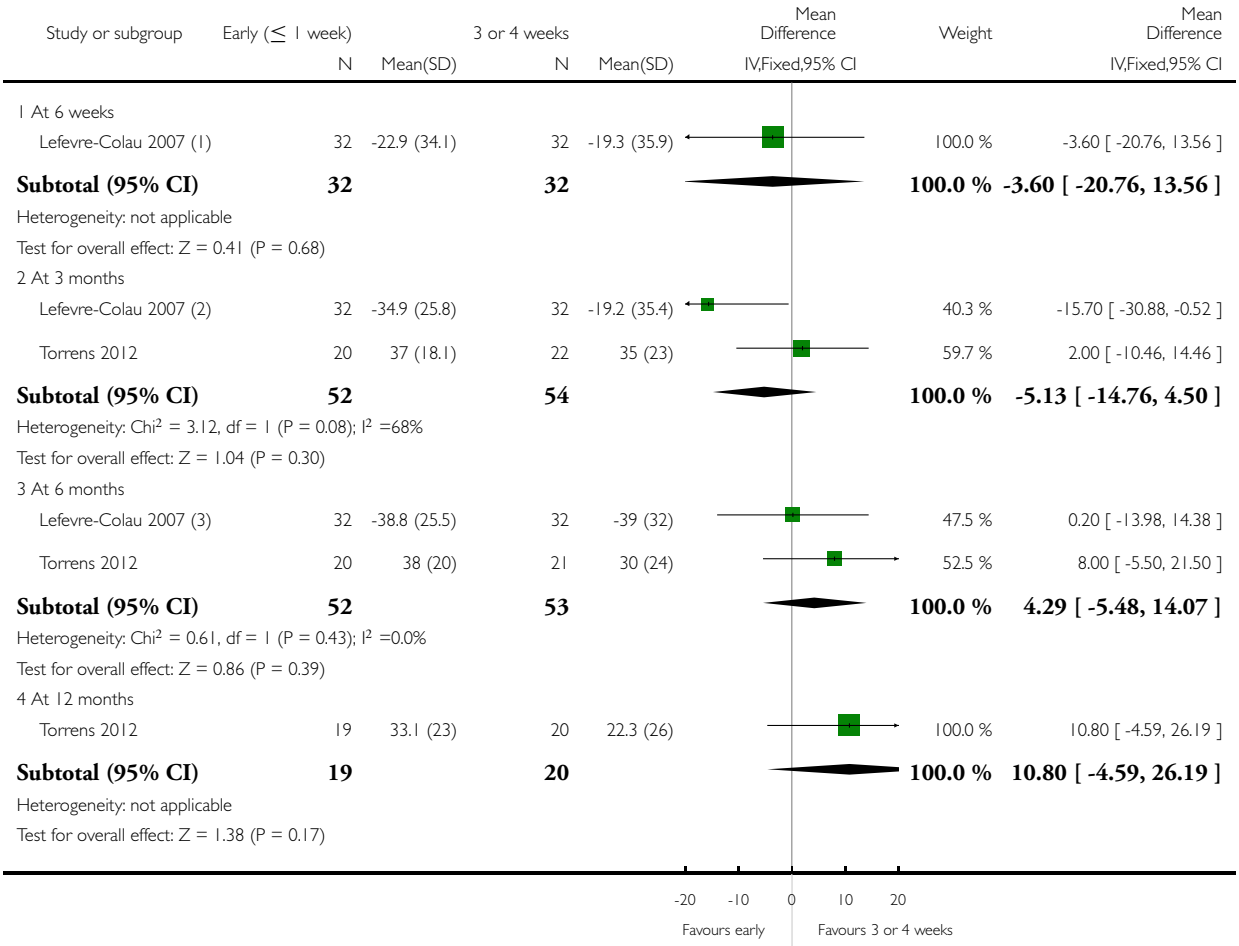


Analysis 1.10. Comparison 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks, Outcome 10 Pain VAS (0 to 100: worst pain).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks

Outcome: 10 Pain VAS (0 to 100: worst pain)



(1) Change score from baseline, multiplied by -1

(2) Change score from baseline, multiplied by -1

(3) Change score from baseline, multiplied by -1

Analysis 1.11. Comparison 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks, Outcome 11 Changes in pain intensity (mm) from baseline: 100 mm visual analogue scale (positive change = less pain).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks

Outcome: 11 Changes in pain intensity (mm) from baseline: 100 mm visual analogue scale (positive change = less pain)

Study or subgroup	Early (≤ 1 week) N	Mean(SD)	3 or 4 weeks N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 At 6 weeks						
Lefevre-Colau 2007	32	22.9 (34.1)	32	19.3 (35.9)		3.60 [-13.56, 20.76]
2 At 3 months						
Lefevre-Colau 2007	32	34.9 (25.8)	32	19.2 (35.4)		15.70 [0.52, 30.88]
3 At 6 months						
Lefevre-Colau 2007	32	38.8 (25.5)	32	39 (32)		-0.20 [-14.38, 13.98]

Analysis 1.12. Comparison 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks, Outcome 12 Range of motion at 6 months (degrees): difference between two shoulders.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks

Outcome: 12 Range of motion at 6 months (degrees): difference between two shoulders

Study or subgroup	Early (≤ 1 week) N	Mean(SD)	3 or 4 weeks N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Abduction						
Lefevre-Colau 2007	32	10.5 (12)	32	17.1 (23.1)		-6.60 [-15.62, 2.42]
2 Anterior elevation						
Lefevre-Colau 2007	32	10.6 (11.3)	32	14.2 (14.5)		-3.60 [-9.97, 2.77]
3 Lateral rotation						
Lefevre-Colau 2007	32	11.7 (10.6)	32	14.2 (16.2)		-2.50 [-9.21, 4.21]

Analysis 1.13. Comparison 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks, Outcome 13 Patient dissatisfied with treatment.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks

Outcome: 13 Patient dissatisfied with treatment

Study or subgroup	Early (≤ 1 week) n/N	3 or 4 weeks n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Lefevre-Colau 2007	1/32	2/32		0.50 [0.05, 5.24]

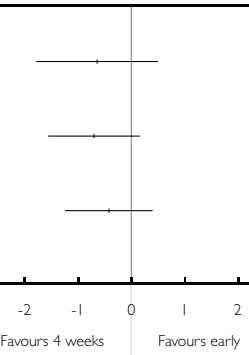
Analysis 1.14. Comparison 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks, Outcome 14 Patient satisfaction (0 to 10: higher scores - greater satisfaction).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 1 Early mobilisation (within or up to 1 week) versus immobilisation for 3 or 4 weeks

Outcome: 14 Patient satisfaction (0 to 10: higher scores - greater satisfaction)

Study or subgroup	Early (≤ 1 week) N	Mean(SD)	3 or 4 weeks N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 At 3 months						
Torrens 2012	20	7.45 (2.1)	22	8.1 (1.6)		-0.65 [-1.79, 0.49]
2 At 6 months						
Torrens 2012	20	8.1 (1.7)	21	8.8 (1)		-0.70 [-1.56, 0.16]
3 At 12 months						
Torrens 2012	19	8.14 (0.95)	20	8.56 (1.6)		-0.42 [-1.24, 0.40]



Analysis 2.1. Comparison 2 Gilchrist bandage versus 'Classic' Desault bandage, Outcome 1 Problems with bandages.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 2 Gilchrist bandage versus 'Classic' Desault bandage

Outcome: 1 Problems with bandages

Study or subgroup	Gilchrist n/N	Desault n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Application of bandage was uncomfortable				
Rommens 1993	4/14	7/14		0.57 [0.21, 1.52]
2 Premature bandage removal				
Rommens 1993	0/14	2/12		0.17 [0.01, 3.29]

Analysis 2.2. Comparison 2 Gilchrist bandage versus 'Classic' Desault bandage, Outcome 2 Fracture displacement by 3 weeks.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 2 Gilchrist bandage versus 'Classic' Desault bandage

Outcome: 2 Fracture displacement by 3 weeks

Study or subgroup	Gilchrist n/N	Desault n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Rommens 1993	2/14	0/12		4.33 [0.23, 82.31]

Analysis 2.3. Comparison 2 Gilchrist bandage versus 'Classic' Desault bandage, Outcome 3 Poor or bad rating by patient at fracture consolidation.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 2 Gilchrist bandage versus 'Classic' Desault bandage

Outcome: 3 Poor or bad rating by patient at fracture consolidation

Study or subgroup	Gilchrist n/N	Desault n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Rommens 1993	2/14	8/14		0.25 [0.06, 0.97]

Analysis 3.1. Comparison 3 Instructed self-exercise versus conventional physiotherapy, Outcome 1 Pain at one year (scale 0 to 8: maximum pain).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 3 Instructed self-exercise versus conventional physiotherapy

Outcome: 1 Pain at one year (scale 0 to 8: maximum pain)

Study or subgroup	Instructions		Physiotherapy		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI	IV,Fixed,95% CI
Bertoft 1984	7	0.6 (1)	6	1 (1.7)		-0.40 [-1.95, 1.15]

Analysis 3.2. Comparison 3 Instructed self-exercise versus conventional physiotherapy, Outcome 2 Severe or moderate pain at 3 months.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 3 Instructed self-exercise versus conventional physiotherapy

Outcome: 2 Severe or moderate pain at 3 months

Study or subgroup	Instructions	Physiotherapy	Risk Ratio	Risk Ratio
	n/N	n/N	M-H,Fixed,95% CI	M-H,Fixed,95% CI
Lundberg 1979	4/20	2/22		2.20 [0.45, 10.74]

Analysis 3.3. Comparison 3 Instructed self-exercise versus conventional physiotherapy, Outcome 3 Requested change of therapy.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 3 Instructed self-exercise versus conventional physiotherapy

Outcome: 3 Requested change of therapy

Study or subgroup	Instructions n/N	Physiotherapy n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Bertoft 1984	1/10	2/8		0.40 [0.04, 3.66]

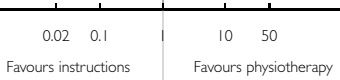
Analysis 3.4. Comparison 3 Instructed self-exercise versus conventional physiotherapy, Outcome 4 Adverse events (frozen shoulder: 1 v 2; unexplained prolonged pain: 0 v 1).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 3 Instructed self-exercise versus conventional physiotherapy

Outcome: 4 Adverse events (frozen shoulder: 1 v 2; unexplained prolonged pain: 0 v 1)

Study or subgroup	Instructions n/N	Physiotherapy n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Lundberg 1979	1/20	3/22		0.37 [0.04, 3.25]



Analysis 3.5. Comparison 3 Instructed self-exercise versus conventional physiotherapy, Outcome 5 Neer's rating (0 to 100: best) at mean 16 months (exploratory analysis).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 3 Instructed self-exercise versus conventional physiotherapy

Outcome: 5 Neer's rating (0 to 100: best) at mean 16 months (exploratory analysis)

Study or subgroup	Instructions		Physiotherapy		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI	IV,Fixed,95% CI
Lundberg 1979	20	83.5 (22.36)	22	86.6 (19.7)		-3.10 [-15.90, 9.70]

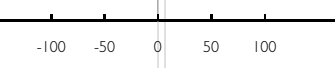
Analysis 3.6. Comparison 3 Instructed self-exercise versus conventional physiotherapy, Outcome 6 Active gleno-humeral elevation (degrees).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 3 Instructed self-exercise versus conventional physiotherapy

Outcome: 6 Active gleno-humeral elevation (degrees)

Study or subgroup	Instructions		Physiotherapy		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI	IV,Fixed,95% CI
Lundberg 1979	20	59.3 (17)	22	59.52 (20.64)		-0.22 [-11.62, 11.18]

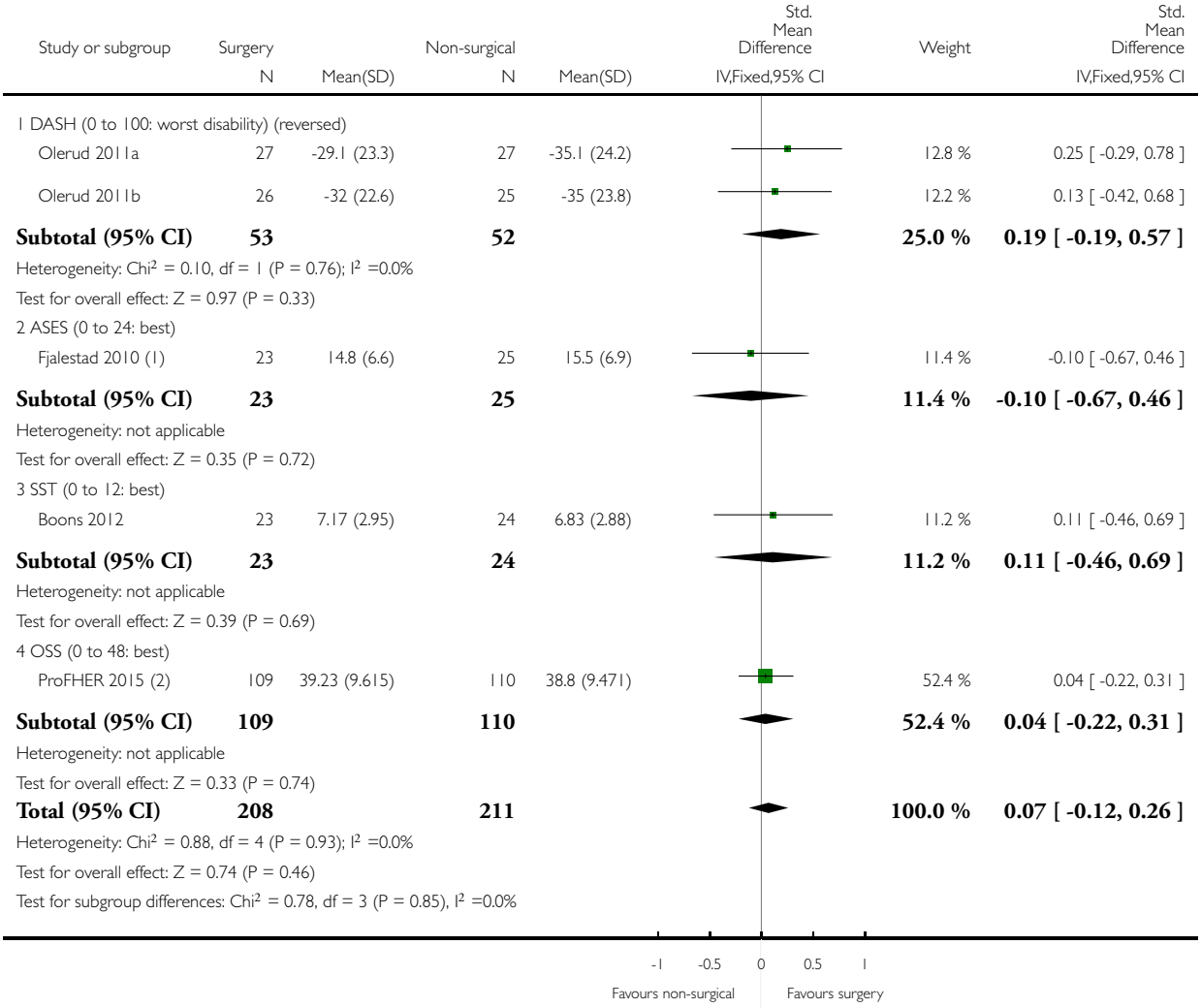


Analysis 4.1. Comparison 4 Surgical versus non-surgical treatment, Outcome 1 Functional scores at 12 months (higher = better outcome).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 1 Functional scores at 12 months (higher = better outcome)



(1) Values made negative to reverse order of effect

(2) Adjusted scores

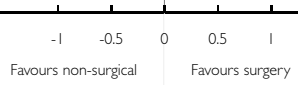
Analysis 4.2. Comparison 4 Surgical versus non-surgical treatment, Outcome 2 Functional scores at 24 months (higher = better outcome).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 2 Functional scores at 24 months (higher = better outcome)

Study or subgroup	Surgery N	Mean(SD)	Non-surgical N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
1 DASH (0 to 100: worst disability) (reversed)							
Olerud 2011a	26	-26.4 (25.2)	25	-35 (26.8)		14.4 %	0.33 [-0.23, 0.88]
Olerud 2011b	24	-30.2 (18.3)	24	-36.9 (21.3)		13.5 %	0.33 [-0.24, 0.90]
Subtotal (95% CI)	**50**		**49**			**27.9 %**	**0.33 [-0.07, 0.73]**
Heterogeneity: Chi^2 = 0.00, df = 1 (P = 0.99); I^2 =0.0%							
Test for overall effect: Z = 1.62 (P = 0.10)							
2 ASES (0 to 24: best)							
Fjalestad 2010	23	14.8 (6.6)	19	14.9 (5.9)		11.9 %	-0.02 [-0.62, 0.59]
Subtotal (95% CI)	**23**		**19**			**11.9 %**	**-0.02 [-0.62, 0.59]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.05 (P = 0.96)							
3 OSS (0 to 48: best)							
ProFHER 2015 (1)	104	40.11 (9.522)	106	40.4 (9.298)		60.1 %	-0.03 [-0.30, 0.24]
Subtotal (95% CI)	**104**		**106**			**60.1 %**	**-0.03 [-0.30, 0.24]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.22 (P = 0.82)							
Total (95% CI)	**177**		**174**			**100.0 %**	**0.07 [-0.14, 0.28]**
Heterogeneity: Chi^2 = 2.24, df = 3 (P = 0.52); I^2 =0.0%							
Test for overall effect: Z = 0.67 (P = 0.50)							
Test for subgroup differences: Chi^2 = 2.24, df = 2 (P = 0.33), I^2 =11%							



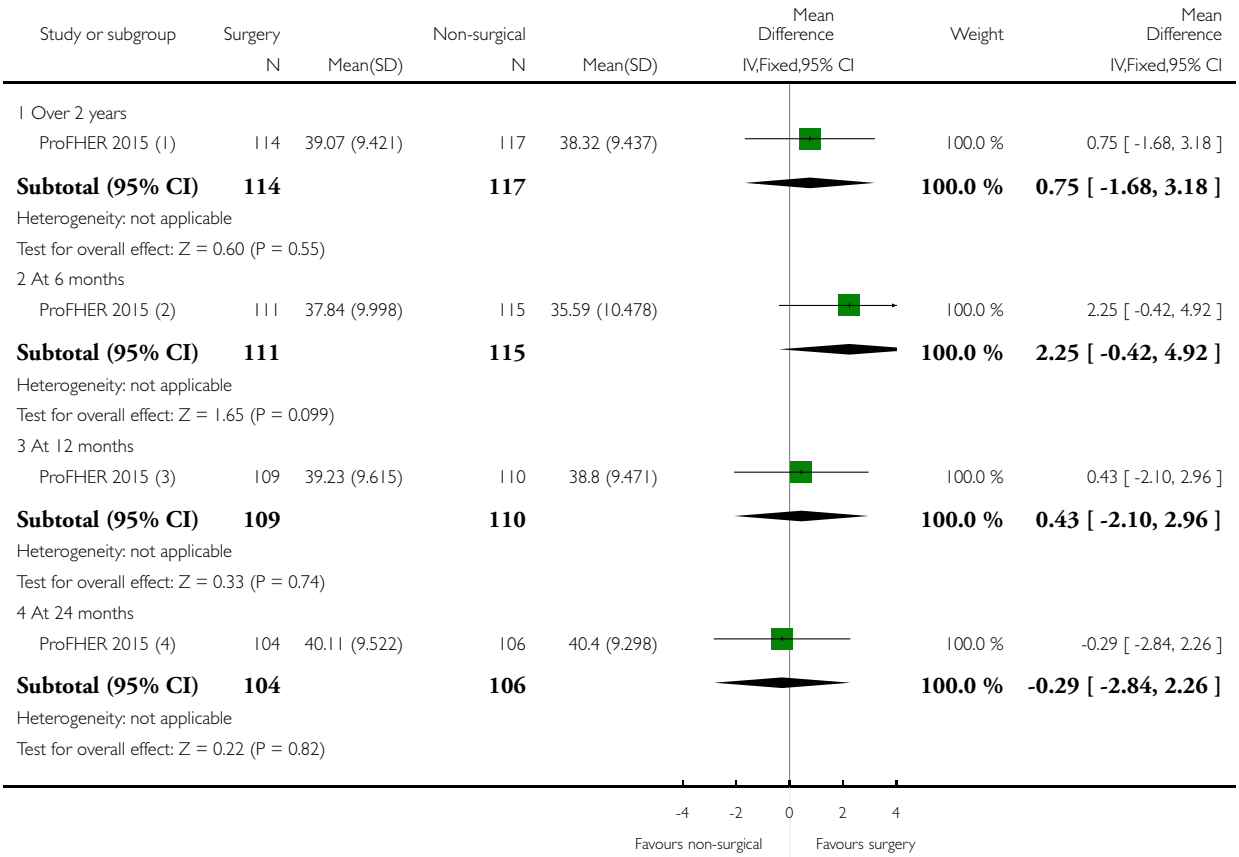
(1) Adjusted scores

Analysis 4.3. Comparison 4 Surgical versus non-surgical treatment, Outcome 3 Oxford Shoulder Score (0 to 48: best outcome).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 3 Oxford Shoulder Score (0 to 48: best outcome)



(1) Adjusted scores for covariates

(2) Adjusted scores

(3) Adjusted scores

(4) Adjusted scores

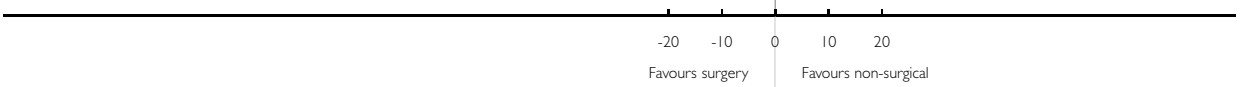
Analysis 4.4. Comparison 4 Surgical versus non-surgical treatment, Outcome 4 DASH (0 to 100: worst disability).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 4 DASH (0 to 100: worst disability)

Study or subgroup	Surgery N	Mean(SD)	Non-surgical N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 at 4 months							
Olerud 2011a	26	36.2 (22.4)	28	35.7 (20.1)		48.3 %	0.50 [-10.88, 11.88]
Olerud 2011b	27	42.8 (20.6)	25	41.5 (19.9)		51.7 %	1.30 [-9.71, 12.31]
Subtotal (95% CI)	**53**		**53**			**100.0 %**	**0.91 [-7.00, 8.83]**
Heterogeneity: Chi^2 = 0.01, df = 1 (P = 0.92); I^2 =0.0%							
Test for overall effect: Z = 0.23 (P = 0.82)							
2 at 12 months							
Olerud 2011b	26	32 (22.6)	25	35 (23.8)		49.7 %	-3.00 [-15.75, 9.75]
Olerud 2011a	27	29.1 (23.3)	27	35.1 (24.2)		50.3 %	-6.00 [-18.67, 6.67]
Subtotal (95% CI)	**53**		**52**			**100.0 %**	**-4.51 [-13.50, 4.48]**
Heterogeneity: Chi^2 = 0.11, df = 1 (P = 0.74); I^2 =0.0%							
Test for overall effect: Z = 0.98 (P = 0.33)							
3 at 24 months							
Olerud 2011a	26	26.4 (25.2)	25	35 (26.8)		38.2 %	-8.60 [-22.89, 5.69]
Olerud 2011b	24	30.2 (18.3)	24	36.9 (21.3)		61.8 %	-6.70 [-17.93, 4.53]
Subtotal (95% CI)	**50**		**49**			**100.0 %**	**-7.43 [-16.26, 1.41]**
Heterogeneity: Chi^2 = 0.04, df = 1 (P = 0.84); I^2 =0.0%							
Test for overall effect: Z = 1.65 (P = 0.099)							



Analysis 4.5. Comparison 4 Surgical versus non-surgical treatment, Outcome 5 American Shoulder and Elbow Surgeons score (0 to 24: best).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 5 American Shoulder and Elbow Surgeons score (0 to 24: best)

Study or subgroup	Surgery N	Mean(SD)	Non-surgical N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 at 6 months						
Fjalestad 2010	23	13.5 (6.6)	25	13.4 (6.7)		0.10 [-3.66, 3.86]
2 at 12 months						
Fjalestad 2010	23	14.8 (6.6)	25	15.5 (6.9)		-0.70 [-4.52, 3.12]
3 at 24 months						
Fjalestad 2010	23	14.8 (6.6)	19	14.9 (5.9)		-0.10 [-3.88, 3.68]

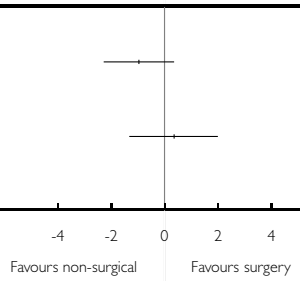
Analysis 4.6. Comparison 4 Surgical versus non-surgical treatment, Outcome 6 Simple Shoulder Test (0 to 12: best function).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 6 Simple Shoulder Test (0 to 12: best function)

Study or subgroup	Surgery N	Mean(SD)	Non-surgical N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 at 3 months						
Boons 2012	24	4.92 (2.21)	25	5.88 (2.47)		-0.96 [-2.27, 0.35]
2 at 12 months						
Boons 2012	23	7.17 (2.95)	24	6.83 (2.88)		0.34 [-1.33, 2.01]



Analysis 4.7. Comparison 4 Surgical versus non-surgical treatment, Outcome 7 Activities of daily living.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 7 Activities of daily living

Study or subgroup	Surgery n/N	Non-surgical n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Unable to manage personal hygiene at 1 year				
Zyto 1997	6/19	5/19		1.20 [0.44, 3.27]
2 Unable to comb hair at 1 year				
Zyto 1997	3/19	3/19		1.00 [0.23, 4.34]
3 Unable to sleep on fractured side at 1 year				
Zyto 1997	6/19	4/19		1.50 [0.50, 4.48]
4 Unable to carry 5 kg at 1 year				
Zyto 1997	10/19	8/19		1.25 [0.63, 2.46]
5 Unable to manage personal hygiene at 50 months				
Zyto 1997	1/14	4/15		0.27 [0.03, 2.12]
6 Unable to comb hair at 50 months				
Zyto 1997	2/14	3/15		0.71 [0.14, 3.66]
7 Unable to sleep on fractured side at 50 months				
Zyto 1997	3/14	2/15		1.61 [0.31, 8.24]
8 Unable to carry 5 kg at 50 months				
Zyto 1997	5/14	7/15		0.77 [0.32, 1.86]

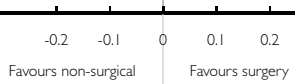
Analysis 4.8. Comparison 4 Surgical versus non-surgical treatment, Outcome 8 Quality of life assessment: EuroQol (0: dead to 1: best health).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 8 Quality of life assessment: EuroQol (0: dead to 1: best health)

Study or subgroup	Surgery N	Mean(SD)	Non-surgical N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 at 3 to 4 months							
Fjalestad 2010	23	0.814 (0.062)	25	0.82 (0.074)		67.0 %	0.00 [-0.04, 0.04]
Olerud 2011a	27	0.71 (0.27)	29	0.61 (0.23)		5.7 %	0.10 [-0.03, 0.23]
Olerud 2011b	27	0.69 (0.22)	25	0.59 (0.28)		5.3 %	0.10 [-0.04, 0.24]
ProFHER 2015	106	0.64 (0.25)	98	0.63 (0.24)		22.0 %	0.01 [-0.06, 0.08]
Subtotal (95% CI)	**183**		**177**			**100.0 %**	**0.01 [-0.02, 0.04]**
Heterogeneity: Chi^2 = 3.87, df = 3 (P = 0.28); I^2 =22%							
Test for overall effect: Z = 0.69 (P = 0.49)							
2 at 6 months							
Fjalestad 2010	23	0.836 (0.083)	25	0.82 (0.088)		54.7 %	0.02 [-0.03, 0.07]
Olerud 2011a	27	0.71 (0.27)	29	0.61 (0.23)		7.4 %	0.10 [-0.03, 0.23]
Olerud 2011b	27	0.69 (0.22)	25	0.59 (0.28)		6.8 %	0.10 [-0.04, 0.24]
ProFHER 2015	111	0.69 (0.25)	114	0.63 (0.24)		31.2 %	0.06 [0.00, 0.12]
Subtotal (95% CI)	**188**		**193**			**100.0 %**	**0.04 [0.01, 0.08]**
Heterogeneity: Chi^2 = 2.59, df = 3 (P = 0.46); I^2 =0.0%							
Test for overall effect: Z = 2.37 (P = 0.018)							
3 at 12 months							
Fjalestad 2010	23	0.841 (0.105)	25	0.82 (0.083)		55.0 %	0.02 [-0.03, 0.08]
Olerud 2011a	27	0.74 (0.24)	27	0.65 (0.28)		8.2 %	0.09 [-0.05, 0.23]
Olerud 2011b	26	0.73 (0.22)	25	0.66 (0.24)		10.0 %	0.07 [-0.06, 0.20]
ProFHER 2015	109	0.65 (0.3)	109	0.68 (0.28)		26.9 %	-0.03 [-0.11, 0.05]
Subtotal (95% CI)	**185**		**186**			**100.0 %**	**0.02 [-0.02, 0.06]**
Heterogeneity: Chi^2 = 3.19, df = 3 (P = 0.36); I^2 =6%							
Test for overall effect: Z = 0.90 (P = 0.37)							
4 at 24 months							
Fjalestad 2010	23	0.849 (0.0984)	19	0.83 (0.0984)		53.0 %	0.02 [-0.04, 0.08]
Olerud 2011a	27	0.7 (0.34)	26	0.59 (0.35)		5.5 %	0.11 [-0.08, 0.30]
Olerud 2011b	24	0.81 (0.12)	24	0.65 (0.27)		13.6 %	0.16 [0.04, 0.28]



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Study or subgroup	Surgery N	Mean(SD)	Non-surgical N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
ProFHER 2015	108	0.67 (0.3)	103	0.69 (0.31)		27.9 %	-0.02 [-0.10, 0.06]
Subtotal (95% CI)	**182**		**172**			**100.0 %**	**0.03 [-0.01, 0.08]**

Heterogeneity: Chi^2 = 6.76, df = 3 (P = 0.08); I^2 =56%

Test for overall effect: Z = 1.57 (P = 0.12)

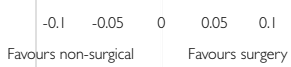
Analysis 4.9. Comparison 4 Surgical versus non-surgical treatment, Outcome 9 Quality of life assessment (Fjalestad 2010 and 2014 data).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 9 Quality of life assessment (Fjalestad 2010 and 2014 data)

Study or subgroup	Surgery N	Mean(SD)	Non-surgical N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 15D at 3 months (0: death; 1: perfect health)						
Fjalestad 2010	23	0.814 (0.062)	25	0.82 (0.074)		0.00 [-0.04, 0.04]
2 15D at 6 months						
Fjalestad 2010	23	0.836 (0.083)	25	0.82 (0.088)		0.02 [-0.03, 0.07]
3 15D at 12 months						
Fjalestad 2010	23	0.841 (0.105)	25	0.82 (0.083)		0.02 [-0.03, 0.08]
4 number of QALYs at 1 year						
Fjalestad 2010	25	0.837 (0.076)	25	0.82 (0.082)		0.02 [-0.02, 0.06]
5 numbers of QALYs at 1 year (- deaths)						
Fjalestad 2010	23	0.841 (0.105)	25	0.82 (0.083)		0.02 [-0.03, 0.08]
6 15D at 24 months						
Fjalestad 2010	23	0.849 (0.0984)	19	0.83 (0.0984)		0.02 [-0.04, 0.08]

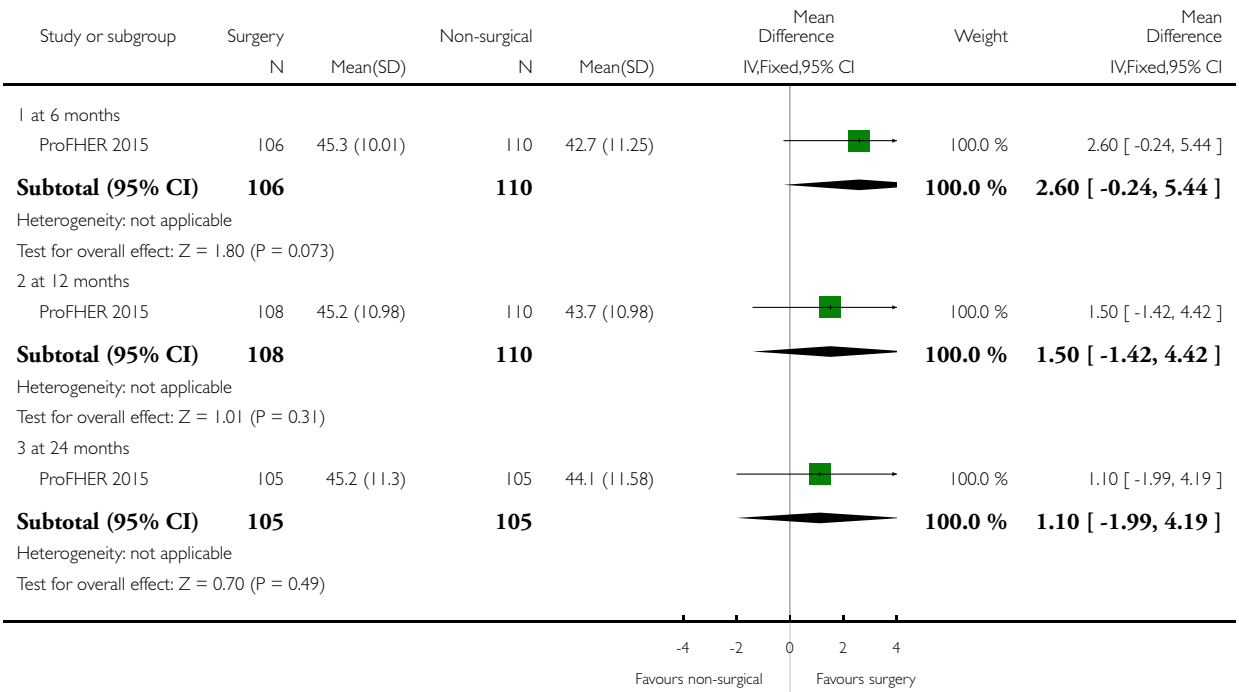


Analysis 4.10. Comparison 4 Surgical versus non-surgical treatment, Outcome 10 Quality of life: SF-12 Physical Component Score (0 to 100: best).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 10 Quality of life: SF-12 Physical Component Score (0 to 100: best)



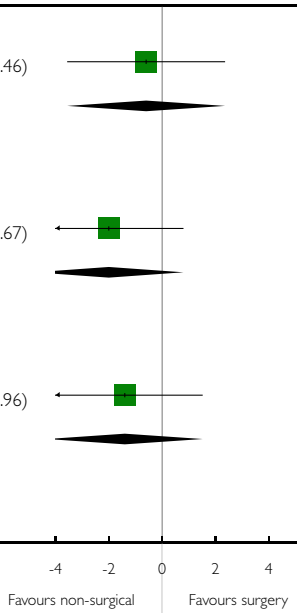
Analysis 4.11. Comparison 4 Surgical versus non-surgical treatment, Outcome 11 Quality of life: SF-12 Mental Component Score (0 to 100: best).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 11 Quality of life: SF-12 Mental Component Score (0 to 100: best)

Study or subgroup	Surgery N	Mean(SD)	Non-surgical N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 at 6 months							
ProFHER 2015	106	49.2 (10.84)	110	49.8 (11.46)		100.0 %	-0.60 [-3.57, 2.37]
Subtotal (95% CI)	**106**		**110**			**100.0 %**	**-0.60 [-3.57, 2.37]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.40 (P = 0.69)							
2 at 12 months							
ProFHER 2015	108	48.8 (10.51)	110	50.8 (10.67)		100.0 %	-2.00 [-4.81, 0.81]
Subtotal (95% CI)	**108**		**110**			**100.0 %**	**-2.00 [-4.81, 0.81]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.39 (P = 0.16)							
3 at 24 months							
ProFHER 2015	105	50.1 (11.64)	105	51.5 (9.96)		100.0 %	-1.40 [-4.33, 1.53]
Subtotal (95% CI)	**105**		**105**			**100.0 %**	**-1.40 [-4.33, 1.53]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.94 (P = 0.35)							



Analysis 4.12. Comparison 4 Surgical versus non-surgical treatment, Outcome 12 Mortality.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 12 Mortality

Study or subgroup	Surgery n/N	Non-surgical n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Boons 2012	0/25	1/25		12.0 %	0.33 [0.01, 7.81]
Fjalestad 2010 (1)	2/25	1/25		8.0 %	2.00 [0.19, 20.67]
Olerud 2011a	2/30	2/29		16.3 %	0.97 [0.15, 6.41]
Olerud 2011b	3/27	2/28		15.7 %	1.56 [0.28, 8.59]
ProFHER 2015	9/125	5/125		40.0 %	1.80 [0.62, 5.22]
Stableforth 1984	1/16	1/16		8.0 %	1.00 [0.07, 14.64]
Total (95% CI)	**248**	**248**		**100.0 %**	**1.40 [0.69, 2.83]**

Total events: 17 (Surgery), 12 (Non-surgical)

Heterogeneity: $Chi^2 = 1.32$, df = 5 (P = 0.93); $I^2 = 0.0\%$

Test for overall effect: Z = 0.94 (P = 0.35)

Test for subgroup differences: Not applicable

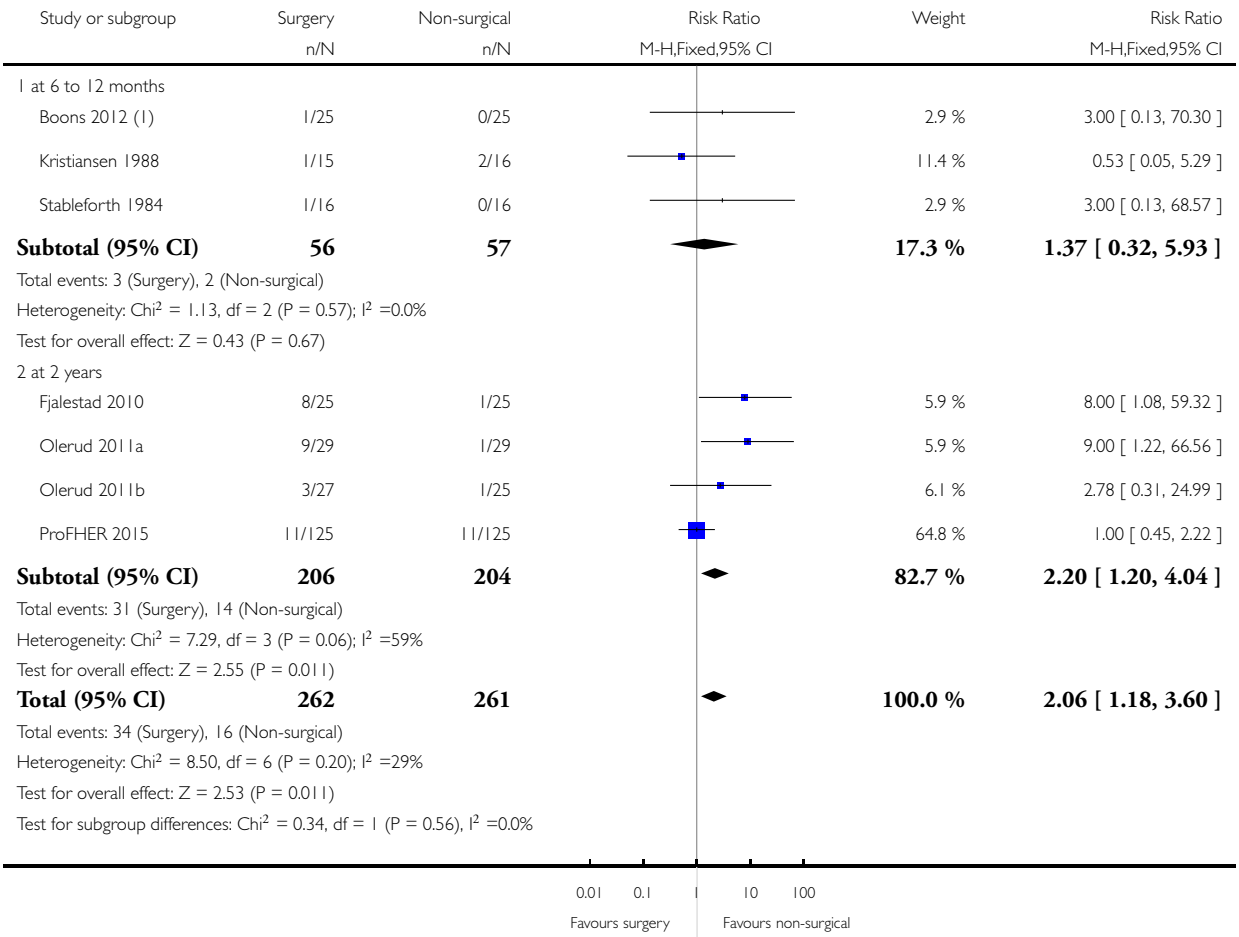
(1) 2 surgery at 8 and 9 weeks; 1 conservative after 1 year

Analysis 4.13. Comparison 4 Surgical versus non-surgical treatment, Outcome 13 Additional surgery (re-operation or secondary surgery).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 13 Additional surgery (re-operation or secondary surgery)



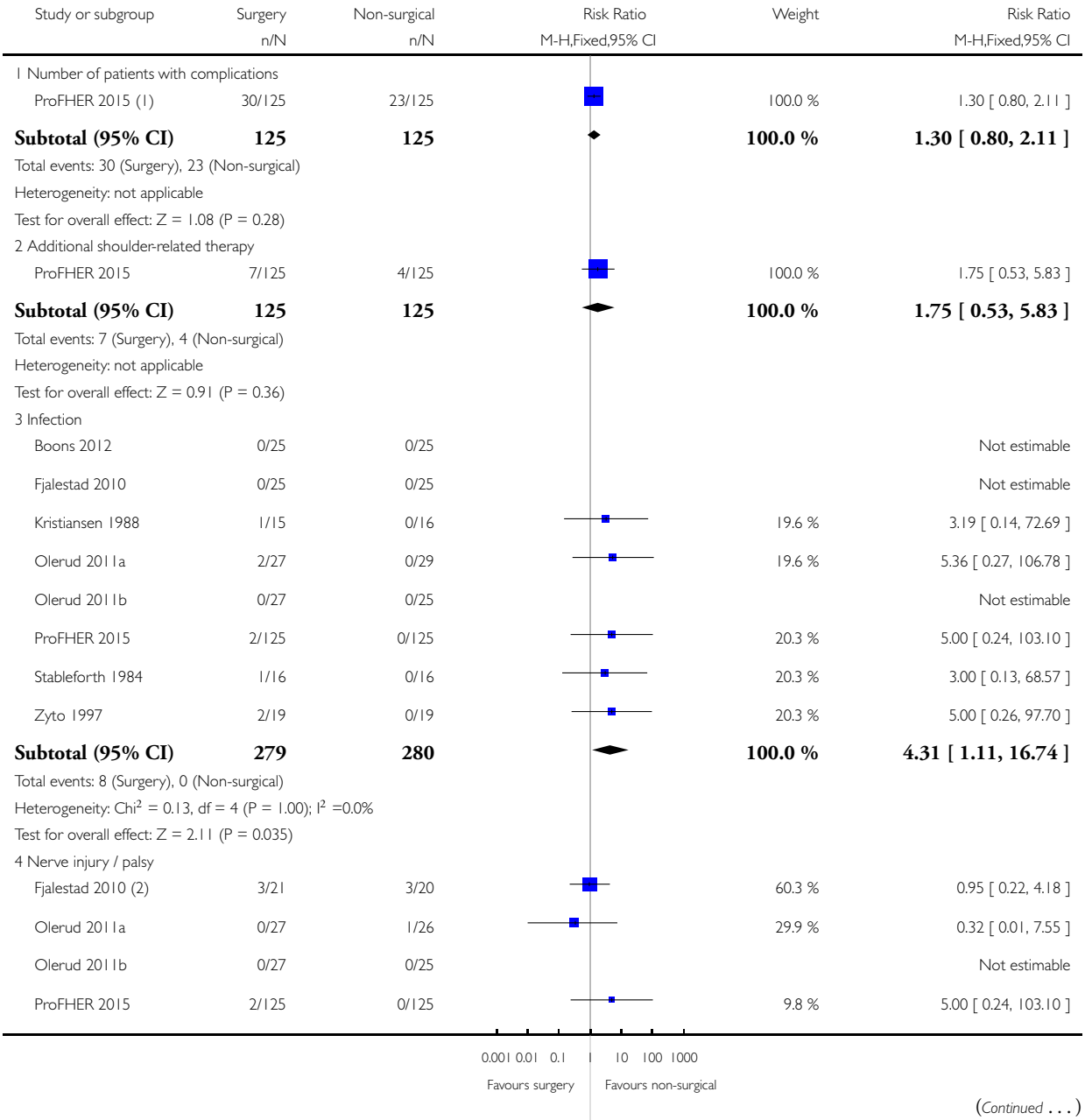
(1) 1 patient in the conservative treatment group had an operation at 13 months from non-union

Analysis 4.14. Comparison 4 Surgical versus non-surgical treatment, Outcome 14 Adverse events / complications.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 14 Adverse events / complications



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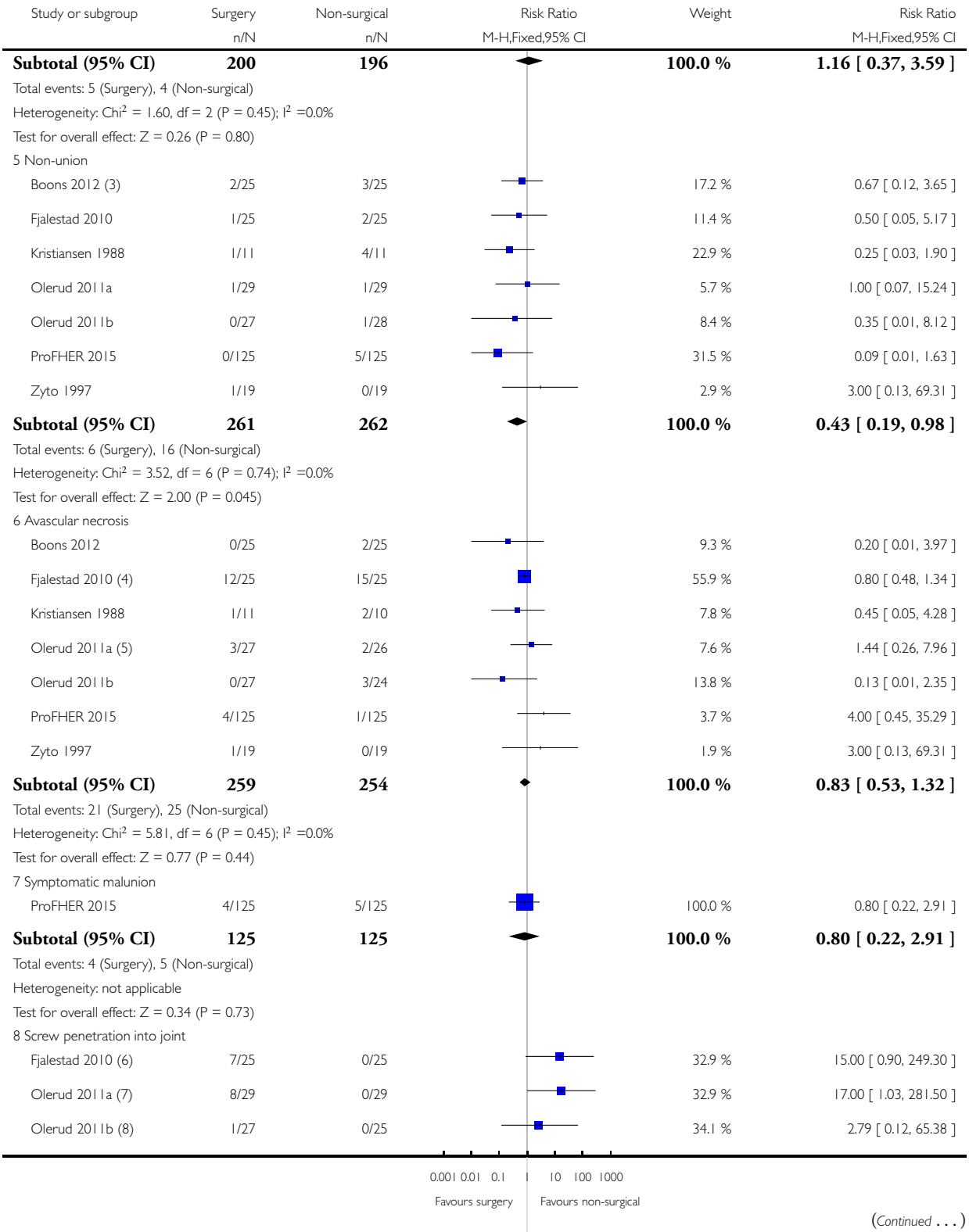

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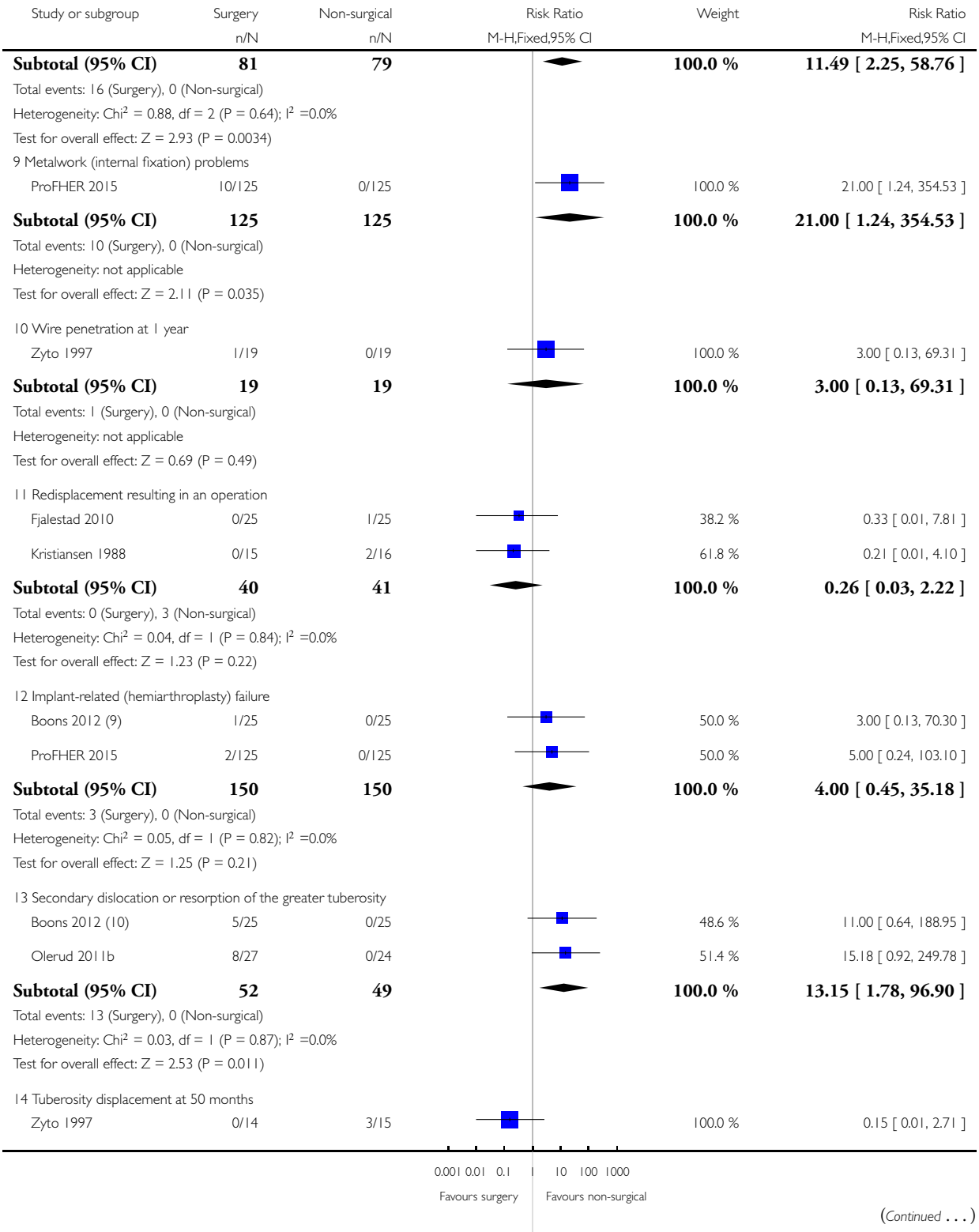

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Study or subgroup	Surgery n/N	Non-surgical n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Subtotal (95% CI)	**14**	**15**		**100.0 %**	**0.15 [0.01, 2.71]**
Total events: 0 (Surgery), 3 (Non-surgical)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.28 (P = 0.20)					
15 Fixation failure resulting in an operation					
Fjalestad 2010	1/25	0/25		100.0 %	3.00 [0.13, 70.30]
Subtotal (95% CI)	**25**	**25**		**100.0 %**	**3.00 [0.13, 70.30]**
Total events: 1 (Surgery), 0 (Non-surgical)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.68 (P = 0.49)					
16 Refracture					
Kristiansen 1988	1/11	1/11		100.0 %	1.00 [0.07, 14.05]
Subtotal (95% CI)	**11**	**11**		**100.0 %**	**1.00 [0.07, 14.05]**
Total events: 1 (Surgery), 1 (Non-surgical)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P = 1.0)					
17 Post-traumatic stiffness					
ProFHER 2015	6/125	5/125		100.0 %	1.20 [0.38, 3.83]
Subtotal (95% CI)	**125**	**125**		**100.0 %**	**1.20 [0.38, 3.83]**
Total events: 6 (Surgery), 5 (Non-surgical)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.31 (P = 0.76)					
18 Impingement					
Olerud 2011a	2/29	1/29		40.0 %	2.00 [0.19, 20.86]
ProFHER 2015	0/125	1/125		60.0 %	0.33 [0.01, 8.10]
Subtotal (95% CI)	**154**	**154**		**100.0 %**	**1.00 [0.18, 5.62]**
Total events: 2 (Surgery), 2 (Non-surgical)					
Heterogeneity: Chi^2 = 0.79, df = 1 (P = 0.37); I^2 =0.0%					
Test for overall effect: Z = 0.0 (P = 1.0)					
19 Rotator cuff tear					
Boons 2012 (11)	1/25	0/25		33.3 %	3.00 [0.13, 70.30]
ProFHER 2015	3/125	1/125		66.7 %	3.00 [0.32, 28.45]
Subtotal (95% CI)	**150**	**150**		**100.0 %**	**3.00 [0.48, 18.73]**
Total events: 4 (Surgery), 1 (Non-surgical)					
Heterogeneity: Chi^2 = 0.0, df = 1 (P = 1.00); I^2 =0.0%					
Test for overall effect: Z = 1.18 (P = 0.24)					
20 Post-traumatic stiffness					
ProFHER 2015	6/125	5/125		100.0 %	1.20 [0.38, 3.83]
Subtotal (95% CI)	**125**	**125**		**100.0 %**	**1.20 [0.38, 3.83]**

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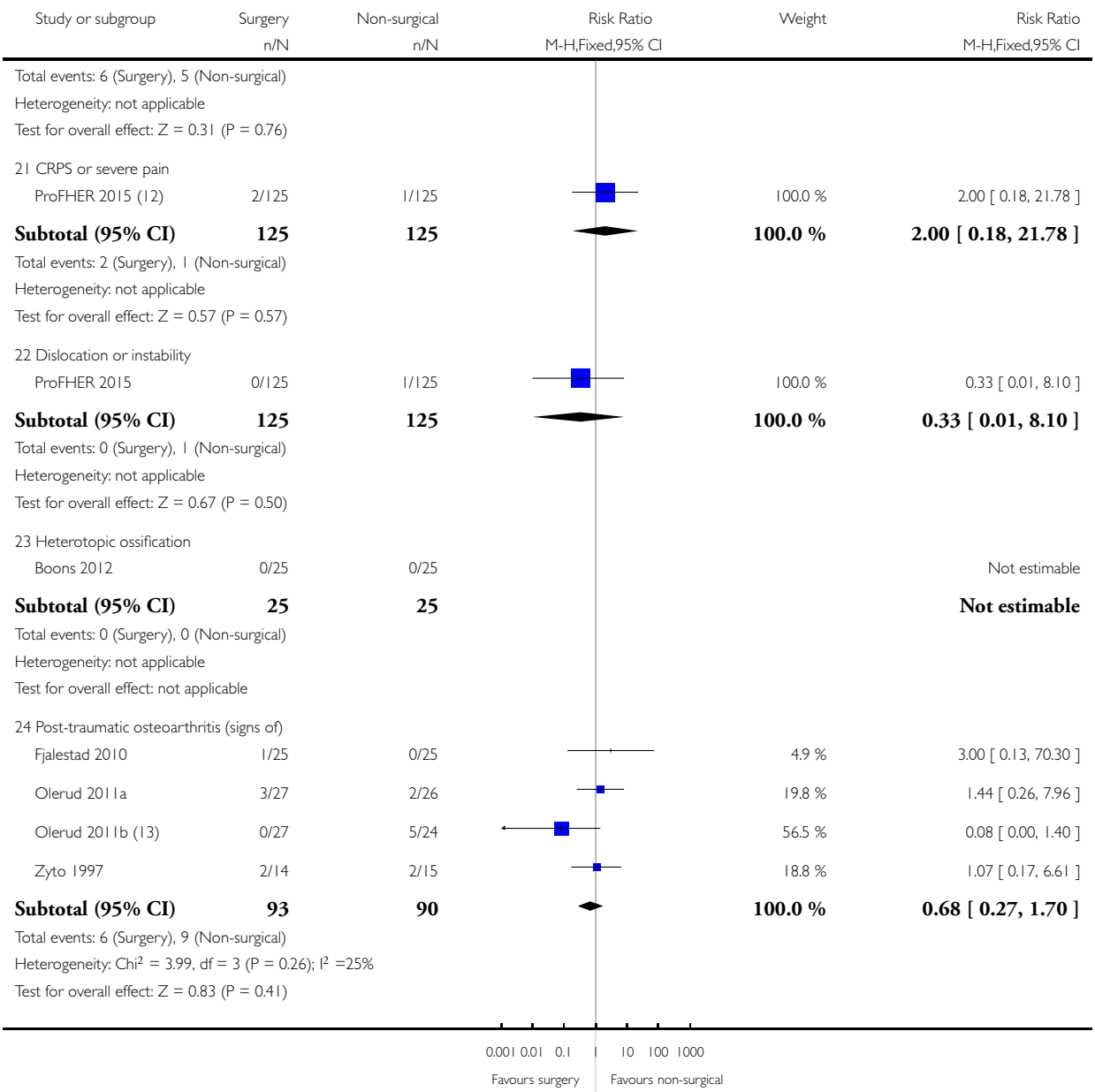


(1) 6 patients in the surgical group had 2 listed complications

(2) 1 person in each group had persistent deltoid atrophy

(3) The 2 non-unions in the surgery group were of the greater tuberosity

(4) At 2 years (8 versus 13 at 1 year): mostly asymptomatic (3 versus 2 had some pain)

(5) 2 cases (1 severe, 1 minor) in the surgical group had reoperations

(6) Three implants were removed

(7) One of the 3 'secondary screw penetrations' were operated on for this reason

(8) 1 patient in this trial had plate fixation instead of a prosthesis

(9) Head-stem separation; revised after 1 week

(10) Secondary superior migration of GT; partial bone resorption in 2

(11) "potential" rotator cuff tear; patient had proximal migration of their hemiarthroplasty

(12) 1 patient in surgery group had complex regional pain syndrome (CRPS)

(13) Surgery was arthroplasty

Analysis 4.15. Comparison 4 Surgical versus non-surgical treatment, Outcome 15 Dependent in activities of daily living (or dead) at 6 months.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 15 Dependent in activities of daily living (or dead) at 6 months

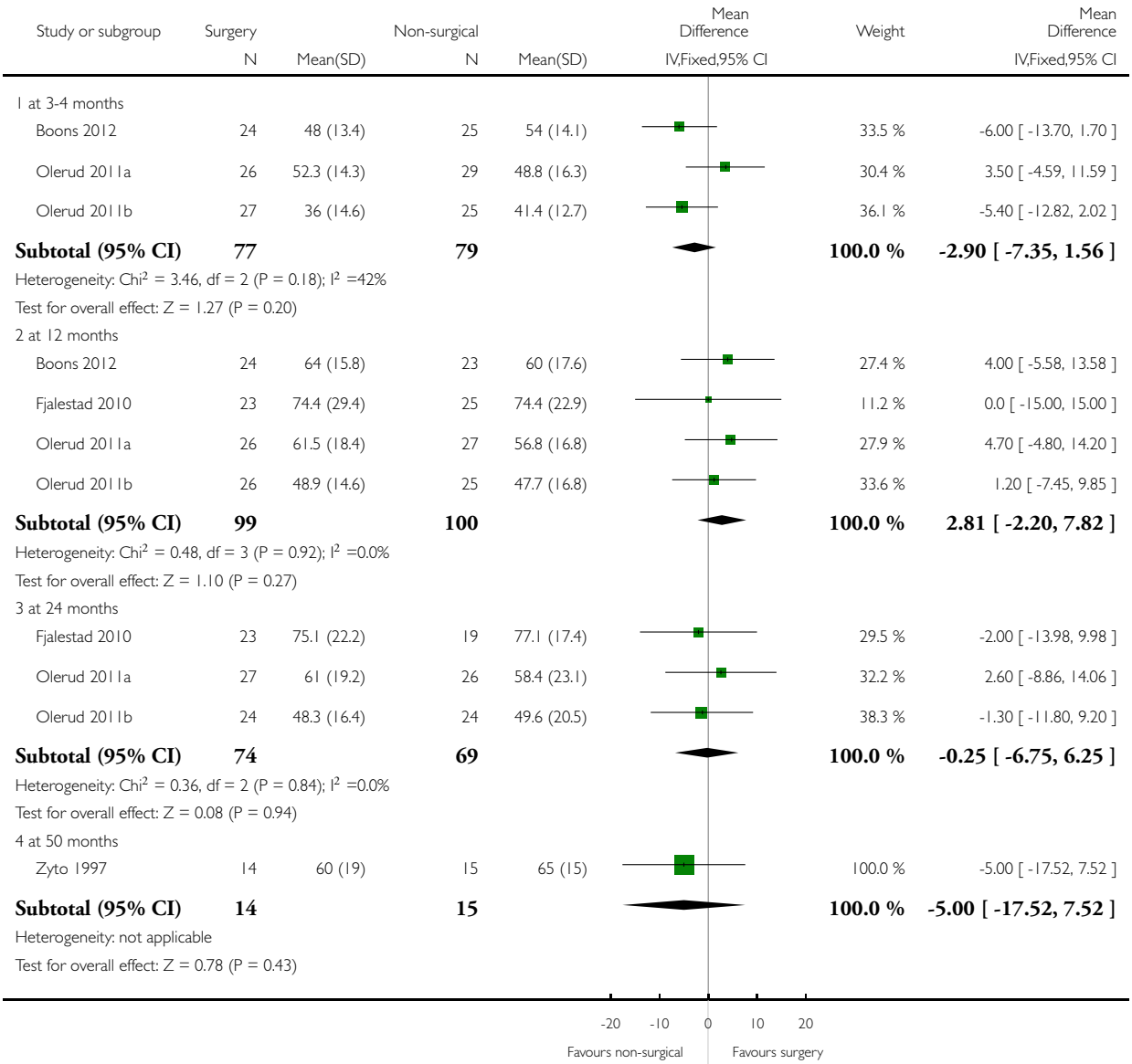
Study or subgroup	Surgery n/N	Non-surgical n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Stableforth 1984	2/16	9/16		0.22 [0.06, 0.87]

Analysis 4.16. Comparison 4 Surgical versus non-surgical treatment, Outcome 16 Constant scores (overall: 0 to 100: best score).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 16 Constant scores (overall: 0 to 100: best score)



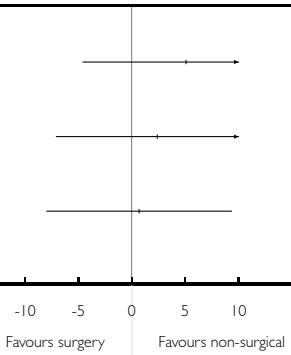
Analysis 4.17. Comparison 4 Surgical versus non-surgical treatment, Outcome 17 Constant scores (difference between injured and uninjured shoulder): Normal = 0..

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 17 Constant scores (difference between injured and uninjured shoulder): Normal = 0.

Study or subgroup	Surgery N	Mean(SD)	Non-surgical N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 at 6 months						
Fjalestad 2010	23	45.6 (15.5)	25	40.5 (18.9)		5.10 [-4.65, 14.85]
2 at 12 months						
Fjalestad 2010	23	35.2 (17.2)	25	32.8 (16.2)		2.40 [-7.07, 11.87]
3 at 24 months						
Fjalestad 2010	23	33.3 (14)	19	32.6 (14.7)		0.70 [-8.04, 9.44]



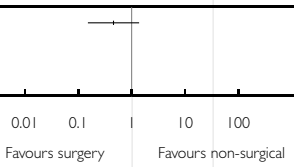
Analysis 4.18. Comparison 4 Surgical versus non-surgical treatment, Outcome 18 Poor or unsatisfactory function at 1 year (Neer rating).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 18 Poor or unsatisfactory function at 1 year (Neer rating)

Study or subgroup	Surgery n/N	Non-surgical n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Kristiansen 1988	3/11	6/10		0.45 [0.15, 1.35]



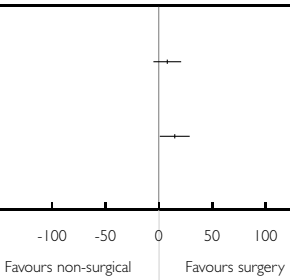
Analysis 4.19. Comparison 4 Surgical versus non-surgical treatment, Outcome 19 VAS disability (0 to 100: no restrictions).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 19 VAS disability (0 to 100: no restrictions)

Study or subgroup	Surgery N	Mean(SD)	Non-surgical N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 at 3 months						
Boons 2012	24	50 (20.6)	25	42 (25.6)		8.00 [-4.99, 20.99]
2 at 12 months						
Boons 2012	24	46 (25.7)	23	31 (24.7)		15.00 [0.59, 29.41]



Analysis 4.20. Comparison 4 Surgical versus non-surgical treatment, Outcome 20 Pain: VAS (0 to 100: worst pain).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 20 Pain: VAS (0 to 100: worst pain)

Study or subgroup	Surgery N	Mean(SD)	Non-surgical N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 At 3 months							
Boons 2012	24	19 (18)	25	37 (21.3)		100.0 %	-18.00 [-29.03, -6.97]
Subtotal (95% CI)	**24**		**25**			**100.0 %**	**-18.00 [-29.03, -6.97]**
Heterogeneity: not applicable							
Test for overall effect: Z = 3.20 (P = 0.0014)							
2 At 2 years							
Olerud 2011a	27	17 (18)	26	20 (22)		51.7 %	-3.00 [-13.84, 7.84]
Olerud 2011b	24	15 (16)	24	25 (23)		48.3 %	-10.00 [-21.21, 1.21]
Subtotal (95% CI)	**51**		**50**			**100.0 %**	**-6.38 [-14.18, 1.41]**
Heterogeneity: Chi^2 = 0.77, df = 1 (P = 0.38); I^2 =0.0%							
Test for overall effect: Z = 1.61 (P = 0.11)							

Analysis 4.21. Comparison 4 Surgical versus non-surgical treatment, Outcome 21 Constant score at 50 months: overall and components.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 21 Constant score at 50 months: overall and components

Study or subgroup	Surgery N	Mean(SD)	Non-surgical N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Overall score (0-100: best score)						
Zyto 1997	14	60 (19)	15	65 (15)		-5.00 [-17.52, 7.52]
2 Pain (maximum score 15)						
Zyto 1997	14	10 (5)	15	12 (3)		-2.00 [-5.03, 1.03]
3 Range of motion (maximum score 40)						
Zyto 1997	14	26 (4)	15	29 (3)		-3.00 [-5.59, -0.41]
4 Power (maximum score 25)						
Zyto 1997	14	8 (5)	15	8 (5)		0.0 [-3.64, 3.64]
5 Activities of daily living (maximum score 20)						
Zyto 1997	14	16 (5)	15	16 (4)		0.0 [-3.31, 3.31]

Analysis 4.22. Comparison 4 Surgical versus non-surgical treatment, Outcome 22 Constant (often severe) pain at 6 months.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 22 Constant (often severe) pain at 6 months

Study or subgroup	Surgery n/N	Non-surgical n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Stableforth 1984	2/15	9/15		0.22 [0.06, 0.86]

Analysis 4.23. Comparison 4 Surgical versus non-surgical treatment, Outcome 23 Failure to recover 75% muscle power relative to other arm (survivors) at 6 months.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 23 Failure to recover 75% muscle power relative to other arm (survivors) at 6 months

Study or subgroup	Surgery n/N	Non-surgical n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Flexion				
Stableforth 1984	3/15	7/15		0.43 [0.14, 1.35]
2 Abduction				
Stableforth 1984	5/15	9/15		0.56 [0.24, 1.27]
3 Lateral rotation				
Stableforth 1984	1/15	7/15		0.14 [0.02, 1.02]

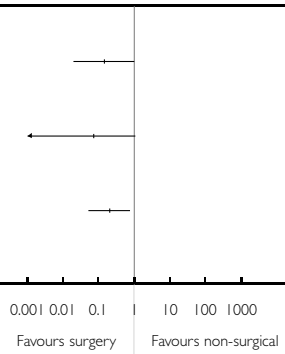
Analysis 4.24. Comparison 4 Surgical versus non-surgical treatment, Outcome 24 Range of movement impairments in survivors at 6 months.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 24 Range of movement impairments in survivors at 6 months

Study or subgroup	Surgery n/N	Non-surgical n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Flexion < 45 degrees				
Stableforth 1984	1/15	7/15		0.14 [0.02, 1.02]
2 Unable to place thumb on mid spine (T12)				
Stableforth 1984	0/15	7/15		0.07 [0.00, 1.07]
3 Lateral rotation < 5 degrees				
Stableforth 1984	2/15	10/15		0.20 [0.05, 0.76]



Analysis 4.25. Comparison 4 Surgical versus non-surgical treatment, Outcome 25 Costs at 1 year (Euros in 2005).

Costs at 1 year (Euros in 2005)

Study	Measure	Surgery	Non-surgical treatment	Difference (conclusion)
Fjalestad 2010	Total health-care costs	mean = 10,367	mean = 10,946	Abstract: "the mean difference in total health-care costs was 597 Euros in favour of surgery (95% CI = -5291, 3777)". No significant difference
Fjalestad 2010	Health-care + indirect costs	mean = 23,953	mean = 21,878	Reformatted text: "Including indirect costs... the difference [was] 2,075 (95% CI = -15,949 to 20,100)". No significant difference, but favours the non-surgical group

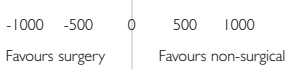
Analysis 4.26. Comparison 4 Surgical versus non-surgical treatment, Outcome 26 Total costs including indirect costs (Euros) at 1 year.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 4 Surgical versus non-surgical treatment

Outcome: 26 Total costs including indirect costs (Euros) at 1 year

Study or subgroup	Surgery N	Mean(SD)	Non-surgical N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Fjalestad 2010	25	23953 (34596)	25	21878 (22696)	2075.00 [-14144.18, 18294.18]	



Analysis 5.1. Comparison 5 Locking plate versus locking intramedullary nail, Outcome 1 American Shoulder and Elbow Surgeons (ASES) score (0 to 100: best).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 5 Locking plate versus locking intramedullary nail

Outcome: 1 American Shoulder and Elbow Surgeons (ASES) score (0 to 100: best)

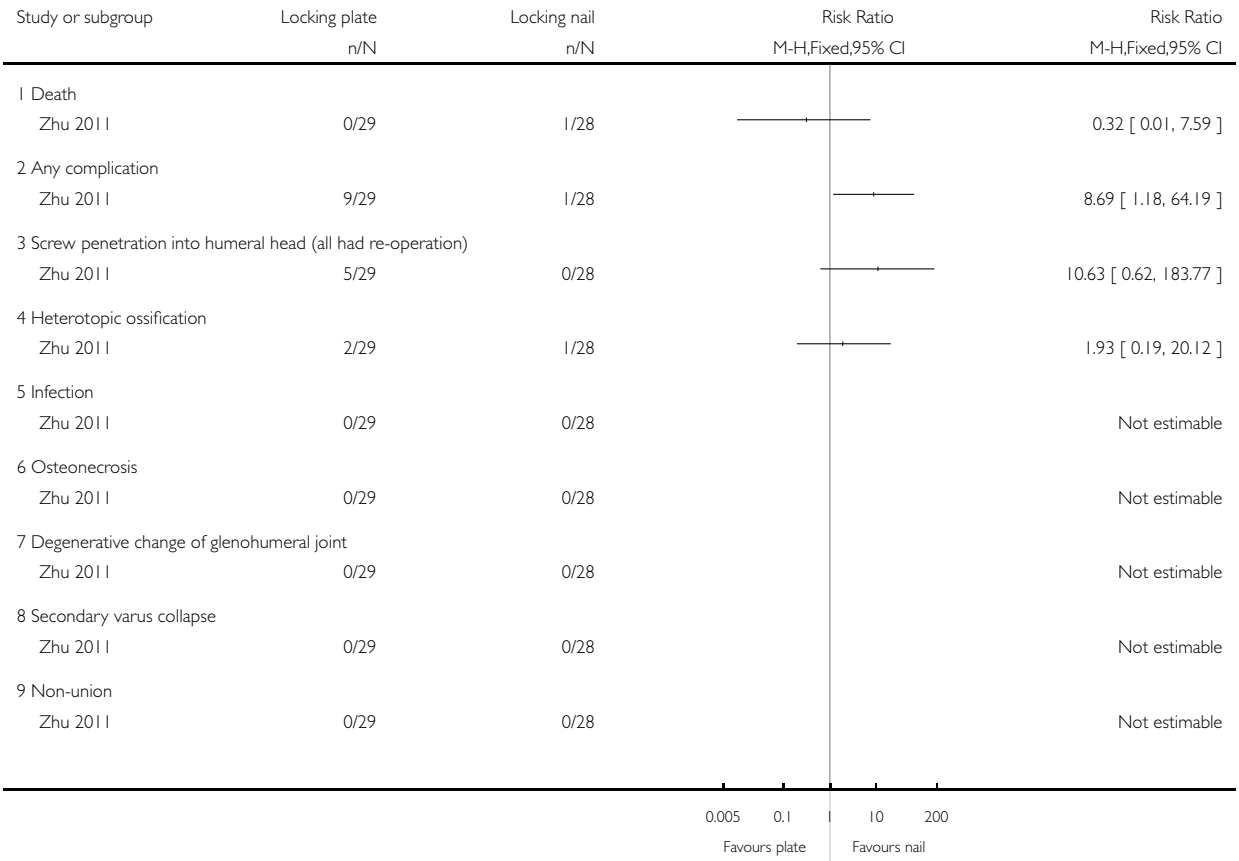
Study or subgroup	Locking plate N	Mean(SD)	Locking nail N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 At 1 year						
Zhu 2011	29	90.8 (9.7)	26	83.6 (11.7)		7.20 [1.48, 12.92]
2 At 3 years						
Zhu 2011	26	94 (6.3)	25	90 (8.1)		4.00 [0.01, 7.99]

Analysis 5.2. Comparison 5 Locking plate versus locking intramedullary nail, Outcome 2 Death, re-operation and adverse events.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 5 Locking plate versus locking intramedullary nail

Outcome: 2 Death, re-operation and adverse events



Analysis 5.3. Comparison 5 Locking plate versus locking intramedullary nail, Outcome 3 Pain (VAS: 0 to 10: worst).

Pain (VAS: 0 to 10: worst)

Study	Measure	Locking plate	Locking nail	Reported significance
Zhu 2011	Pain at 1 year	median = 0.5 interquartile range: 1.8 n = 29	median = 1.0 interquartile range = 1.0 n = 26	P = 0.042

Pain (VAS: 0 to 10: worst) (*Continued*)

Zhu 2011	Pain at 3 years	median = 0 interquartile range = 0.8 n = 26	median = 0 interquartile range = 1.0 n = 25	P = 0.642

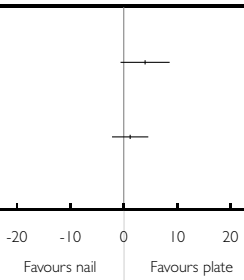
Analysis 5.4. Comparison 5 Locking plate versus locking intramedullary nail, Outcome 4 Constant score (0 to 100: best).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 5 Locking plate versus locking intramedullary nail

Outcome: 4 Constant score (0 to 100: best)

Study or subgroup	Locking plate N	Mean(SD)	Locking nail N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 At 1 year						
Zhu 2011	29	92 (6.3)	26	88 (10.4)		4.00 [-0.61, 8.61]
2 At 3 year						
Zhu 2011	26	94.5 (5.8)	25	93.3 (6.7)		1.20 [-2.24, 4.64]



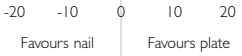
Analysis 5.5. Comparison 5 Locking plate versus locking intramedullary nail, Outcome 5 Active range of motion (at 3 years).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 5 Locking plate versus locking intramedullary nail

Outcome: 5 Active range of motion (at 3 years)

Study or subgroup	Locking plate N	Mean(SD)	Locking nail N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Forward elevation (degrees)						
Zhu 2011	26	157.3 (15.1)	25	160.8 (11.9)		-3.50 [-10.95, 3.95]
2 External rotation						
Zhu 2011	26	40.4 (17.4)	25	47.8 (17.3)		-7.40 [-16.92, 2.12]



Analysis 5.6. Comparison 5 Locking plate versus locking intramedullary nail, Outcome 6 Range of movement: internal rotation (level on spine).

Range of movement: internal rotation (level on spine)

Study	Measure	Locking plate	Locking nail	Reported significance
Zhu 2011	At 1 year	mean location = T8 range = T4 to L2 n = 29	mean location = T9 range = T2 to buttock n = 26	P = 0.443
Zhu 2011	At 3 years	mean location = T8 range = T2 to buttock n = 26	mean location = T8 range = T2 to buttock n = 25	P = 0.636

Analysis 5.7. Comparison 5 Locking plate versus locking intramedullary nail, Outcome 7 Strength of suprapinatus (relative to opposite side) % - at 3 years.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 5 Locking plate versus locking intramedullary nail

Outcome: 7 Strength of suprapinatus (relative to opposite side) % - at 3 years

Study or subgroup	Locking plate N	Mean(SD)	Locking nail N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 At 1 year						
Zhu 2011	29	77.4 (20.8)	26	64.3 (18.3)		13.10 [2.77, 23.43]
2 At 3 years						
Zhu 2011	26	79.3 (20.4)	25	70.2 (16)		9.10 [-0.94, 19.14]

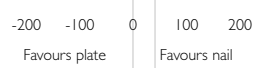
Analysis 5.8. Comparison 5 Locking plate versus locking intramedullary nail, Outcome 8 Operation times and blood loss.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 5 Locking plate versus locking intramedullary nail

Outcome: 8 Operation times and blood loss

Study or subgroup	Locking plate N	Mean(SD)	Locking nail N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Duration of surgery (minutes)						
Zhu 2011	29	109.3 (36)	28	84.4 (36.9)		24.90 [5.97, 43.83]
2 Blood loss (ml)						
Zhu 2011	29	382.1 (200.6)	28	214.1 (140.2)		168.00 [78.41, 257.59]



Analysis 5.9. Comparison 5 Locking plate versus locking intramedullary nail, Outcome 9 Intra-operative complication.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 5 Locking plate versus locking intramedullary nail

Outcome: 9 Intra-operative complication

Study or subgroup	Locking plate n/N	Locking nail n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Pneumothorax				
Zhu 2011	0/29	1/28		0.32 [0.01, 7.59]
2 Blood transfusion				
Zhu 2011	5/29	1/28		4.83 [0.60, 38.77]

Analysis 6.1. Comparison 6 Locking plate versus intramedullary nails (Zifko method), Outcome 1 Complications and [slight] malunion.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 6 Locking plate versus intramedullary nails (Zifko method)

Outcome: 1 Complications and [slight] malunion

Study or subgroup	Locking plate n/N	Intramedually nails n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Any complication				
Smejkal 2011	11/28	9/27		1.18 [0.58, 2.38]
2 Malunion (usually slight)				
Smejkal 2011	7/28	13/27		0.52 [0.24, 1.10]

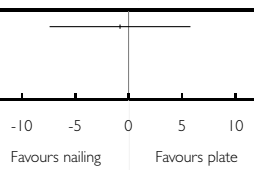
Analysis 6.2. Comparison 6 Locking plate versus intramedullary nails (Zifko method), Outcome 2 Constant score (% of healthy limb) at mean 2 years.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 6 Locking plate versus intramedullary nails (Zifko method)

Outcome: 2 Constant score (% of healthy limb) at mean 2 years

Study or subgroup	Locking plate N	Mean(SD)	Intramedually nails N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Smejkal 2011	28	86.64 (10.83)	27	87.45 (14.03)		-0.81 [-7.45, 5.83]



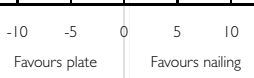
Analysis 6.3. Comparison 6 Locking plate versus intramedullary nails (Zifko method), Outcome 3 Time to union and time to recover upper limb function (weeks).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 6 Locking plate versus intramedullary nails (Zifko method)

Outcome: 3 Time to union and time to recover upper limb function (weeks)

Study or subgroup	Locking plate N	Mean(SD)	Intramedually nails N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Time to radiographic union						
Smejkal 2011	28	16.6 (11.19)	27	14.5 (3.52)		2.10 [-2.25, 6.45]
2 Time to recover normal upper limb function						
Smejkal 2011	28	27.2 (14.16)	27	21.4 (7.52)		5.80 [-0.16, 11.76]



Analysis 6.4. Comparison 6 Locking plate versus intramedullary nails (Zifko method), Outcome 4 Operation and fluoroscopic times.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 6 Locking plate versus intramedullary nails (Zifko method)

Outcome: 4 Operation and fluoroscopic times

Study or subgroup	Locking plate N	Mean(SD)	Intramedually nails N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Duration of operation (minutes)						
Smejkal 2011	28	117.14 (22.12)	27	72.4 (25.05)		44.74 [32.23, 57.25]
2 X-ray exposure (minutes)						
Smejkal 2011	28	4.76 (2.52)	27	6.39 (3.91)		-1.63 [-3.38, 0.12]

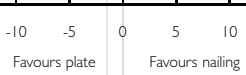
Analysis 6.5. Comparison 6 Locking plate versus intramedullary nails (Zifko method), Outcome 5 Length of hospital stay (days).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 6 Locking plate versus intramedullary nails (Zifko method)

Outcome: 5 Length of hospital stay (days)

Study or subgroup	Locking plate N	Mean(SD)	Intramedually nails N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Smejkal 2011	28	7.5 (3.27)	27	6.3 (2.54)		1.20 [-0.34, 2.74]



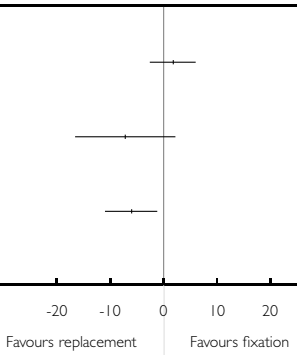
Analysis 7.1. Comparison 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures), Outcome 1 DASH score (0 to 100: worst disability).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures)

Outcome: 1 DASH score (0 to 100: worst disability)

Study or subgroup	Replacement N	Mean(SD)	Fixation N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 At 4 months						
Cai 2012	18	33.4 (6.1)	13	31.7 (6.1)		1.70 [-2.65, 6.05]
2 At 12 months						
Cai 2012	16	21.1 (12.56)	12	28.4 (12.56)		-7.30 [-16.70, 2.10]
3 At 24 months						
Cai 2012 (1)	15	9.2 (6.5)	12	15.3 (6.5)		-6.10 [-11.03, -1.17]



(1) SDs derived from reported P = 0.023 but report states not statistically significant

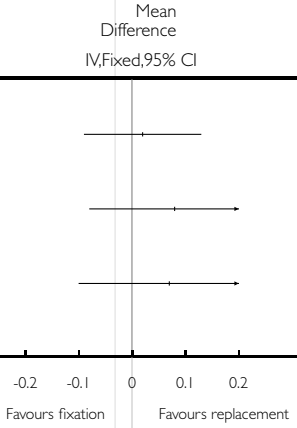
Analysis 7.2. Comparison 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures), Outcome 2 EQ-5D score (0 to 1: best quality of life).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures)

Outcome: 2 EQ-5D score (0 to 1: best quality of life)

Study or subgroup	Replacement N	Mean(SD)	Fixation N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 At 4 months						
Cai 2012	18	0.65 (0.14)	13	0.63 (0.17)		0.02 [-0.09, 0.13]
2 At 12 months						
Cai 2012	16	0.79 (0.24)	12	0.71 (0.19)		0.08 [-0.08, 0.24]
3 At 24 months						
Cai 2012 (1)	15	0.81 (0.17)	12	0.74 (0.26)		0.07 [-0.10, 0.24]



(1) SDs derived from reported P = 0.023 but report states not statistically significant

Analysis 7.3. Comparison 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures), Outcome 3 Re-operation.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures)

Outcome: 3 Re-operation

Study or subgroup	Replacement n/N	Fixation n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Hemiarthroplasty versus tension band wiring					
Hoellen 1997 (1)	0/15	5/15		60.7 %	0.09 [0.01, 1.51]
Subtotal (95% CI)	**15**	**15**		**60.7 %**	**0.09 [0.01, 1.51]**
Total events: 0 (Replacement), 5 (Fixation)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.67 (P = 0.095)					
2 Hemiarthroplasty versus locking plate fixation					
Cai 2012 (2)	3/19	3/13		39.3 %	0.68 [0.16, 2.88]
Subtotal (95% CI)	**19**	**13**		**39.3 %**	**0.68 [0.16, 2.88]**
Total events: 3 (Replacement), 3 (Fixation)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.52 (P = 0.60)					
Total (95% CI)	**34**	**28**		**100.0 %**	**0.32 [0.10, 1.10]**
Total events: 3 (Replacement), 8 (Fixation)					
Heterogeneity: Chi^2 = 1.82, df = 1 (P = 0.18); I^2 =45%					
Test for overall effect: Z = 1.81 (P = 0.070)					
Test for subgroup differences: Chi^2 = 1.57, df = 1 (P = 0.21), I^2 =36%					

(1) At 1 year

(2) At 2 years

Analysis 7.4. Comparison 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures), Outcome 4 Dead at 2 years.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures)

Outcome: 4 Dead at 2 years

Study or subgroup	Replacement n/N	Fixation n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Cai 2012	1/19	0/13		2.10 [0.09, 47.89]

Analysis 7.5. Comparison 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures), Outcome 5 Implant removal at 1 year.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures)

Outcome: 5 Implant removal at 1 year

Study or subgroup	Replacement n/N	Fixation n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Hoellen 1997	0/15	4/15		0.11 [0.01, 1.90]

Analysis 7.6. Comparison 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures), Outcome 6 Constant score (0 to 100: best score).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures)

Outcome: 6 Constant score (0 to 100: best score)

Study or subgroup	Replacement N	Mean(SD)	Fixation N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 At 4 months						
Cai 2012	18	57.8 (12.51)	13	48.4 (12.51)		9.40 [0.48, 18.32]
2 At 12 months						
Cai 2012	16	60.1 (5.1)	12	55.5 (5.1)		4.60 [0.78, 8.42]
3 At 24 months						
Cai 2012	15	72.9 (12.32)	12	60.7 (12.32)		12.20 [2.85, 21.55]

Analysis 7.7. Comparison 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures), Outcome 7 Pain VAS (0 to 100: worst pain) at 24 months.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures)

Outcome: 7 Pain VAS (0 to 100: worst pain) at 24 months

Study or subgroup	Replacement N	Mean(SD)	Fixation N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Cai 2012 (1)	15	13 (47.9)	21	21 (47.9)		-8.00 [-39.74, 23.74]

(1) SDs derived from reported P = 0.023 but report states not statistically significant

Analysis 7.8. Comparison 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures), Outcome 8 Pain at 1 year.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures)

Outcome: 8 Pain at 1 year

Study or subgroup	Replacement n/N	Fixation n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Hoellen 1997	1/9	2/9		0.50 [0.05, 4.58]

Analysis 7.9. Comparison 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures), Outcome 9 Range of motion at 24 months.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 7 Replacement (hemiarthroplasty) versus fixation (tension band wiring; plate fixation) (4 part fractures)

Outcome: 9 Range of motion at 24 months

Study or subgroup	Replacement N	Mean(SD)	Fixation N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Flexion (degrees)						
Cai 2012	15	129 (27.47)	12	117 (27.49)		12.00 [-8.86, 32.86]
2 Extension (degrees)						
Cai 2012 (1)	15	123 (36.98)	12	111 (36.98)		12.00 [-16.07, 40.07]

(1) SDs derived from reported P = 0.023 but report states not statistically significant

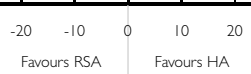
Analysis 8.1. Comparison 8 Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA), Outcome 1 Shoulder function scores at 24 to 49 months.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 8 Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA)

Outcome: 1 Shoulder function scores at 24 to 49 months

Study or subgroup	RSA N	RSA Mean(SD)	HA N	HA Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Quick DASH score (0 to 55: worst outcome)						
Sebasti -Forcada 2014	31	17.5 (7.78)	30	24.4 (7.78)		-6.90 [-10.81, -2.99]



Analysis 8.2. Comparison 8 Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA), Outcome 2 Re-operation.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 8 Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA)

Outcome: 2 Re-operation

Study or subgroup	RSA n/N	HA n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Sebasti -Forcada 2014 (1)	1/31	6/31		0.17 [0.02, 1.30]

(1) All re-operations to RSA

Analysis 8.3. Comparison 8 Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA), Outcome 3 Death.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 8 Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA)

Outcome: 3 Death

Study or subgroup	RSA n/N	HA n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Sebasti -Forcada 2014	0/31	0/31			Not estimable
Total (95% CI)	**31**	**31**			**Not estimable**

Total events: 0 (RSA), 0 (HA)

Heterogeneity: not applicable

Test for overall effect: not applicable

Test for subgroup differences: Not applicable

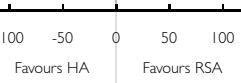
Analysis 8.4. Comparison 8 Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA), Outcome 4 Composite (objective and subjective) shoulder function scores at 24 to 49 months.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 8 Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA)

Outcome: 4 Composite (objective and subjective) shoulder function scores at 24 to 49 months

Study or subgroup	RSA N	Mean(SD)	HA N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 UCLA score (0 to 35: best outcome)						
Sebasti -Forcada 2014	31	29.1 (9.02)	30	21.1 (9.02)		8.00 [3.47, 12.53]
2 Constant score (0 to 100: best outcome)						
Sebasti -Forcada 2014	31	56.1 (18.15)	30	40 (18.15)		16.10 [6.99, 25.21]
3 Constant % relative to opposite side						
Sebasti -Forcada 2014	31	79.7 (26.95)	30	55.8 (26.95)		23.90 [10.37, 37.43]



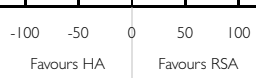
Analysis 8.5. Comparison 8 Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA), Outcome 5 Constant score at 24 to 49 months: overall and components.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 8 Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA)

Outcome: 5 Constant score at 24 to 49 months: overall and components

Study or subgroup	RSA N	Mean(SD)	HA N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Overall score (0-100: best score)						
Sebasti -Forcada 2014	31	56.1 (18.15)	30	40 (18.15)		16.10 [6.99, 25.21]
2 Pain (maximum score 15)						
Sebasti -Forcada 2014	31	14 (5.86)	30	8.8 (5.86)		5.20 [2.26, 8.14]
3 Range of motion (maximum score 40)						
Sebasti -Forcada 2014	31	21.7 (7.67)	30	14.9 (7.67)		6.80 [2.95, 10.65]
4 Power (maximum score 25)						
Sebasti -Forcada 2014	31	4.8 (3.04)	30	2.1 (3.04)		2.70 [1.17, 4.23]
5 Activities of daily living (maximum score 20)						
Sebasti -Forcada 2014	31	16.7 (5.07)	30	12.2 (5.05)		4.50 [1.96, 7.04]



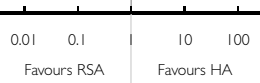
Analysis 8.6. Comparison 8 Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA), Outcome 6 Complications.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 8 Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA)

Outcome: 6 Complications

Study or subgroup	RSA n/N	HA n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Any complication				
Sebasti -Forcada 2014	2/31	10/30		0.19 [0.05, 0.81]
2 Intra-operative fracture				
Sebasti -Forcada 2014 (1)	0/31	1/30		0.32 [0.01, 7.63]
3 Deep infection				
Sebasti -Forcada 2014 (2)	1/31	0/30		2.91 [0.12, 68.66]
4 Superficial infection				
Sebasti -Forcada 2014 (3)	0/31	1/30		0.32 [0.01, 7.63]
5 Haematoma				
Sebasti -Forcada 2014 (4)	1/31	0/30		2.91 [0.12, 68.66]
6 Neurological complications				
Sebasti -Forcada 2014	0/31	1/30		0.32 [0.01, 7.63]
7 Severe stiffness				
Sebasti -Forcada 2014 (5)	0/31	1/30		0.32 [0.01, 7.63]
8 Proximal migration of implant				
Sebasti -Forcada 2014 (6)	0/31	6/31		0.08 [0.00, 1.31]



(1) Treated with wire cerclage

(2) Two stage revision to another RSA

(3) Resolved with antibiotics

(4) Resolved with conservative treatment

(5) Had manipulation under anaesthesia

(6) All had severe pain and limited function and had revision to RSA

Analysis 8.7. Comparison 8 Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA), Outcome 7 Radiological assessment findings.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 8 Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA)

Outcome: 7 Radiological assessment findings

Study or subgroup	RSA n/N	HA n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Malunion of tuberosities				
Sebasti -Forcada 2014	6/31	4/30		1.45 [0.45, 4.64]
2 Resorption of tuberosities				
Sebasti -Forcada 2014	5/31	9/30		0.54 [0.20, 1.42]
3 Scapular notching				
Sebasti -Forcada 2014 (1)	1/31	0/30		2.91 [0.12, 68.66]
4 Heterotopic ossification				
Sebasti -Forcada 2014 (2)	5/31	6/31		0.83 [0.28, 2.45]

(1) No clinical effect

(2) No clinical significance

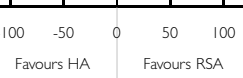
Analysis 8.8. Comparison 8 Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA), Outcome 8 Range of motion (degrees) at 24 to 49 months.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 8 Reverse shoulder arthroplasty (RSA) versus hemiarthroplasty (HA)

Outcome: 8 Range of motion (degrees) at 24 to 49 months

Study or subgroup	RSA N	Mean(SD)	HA N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Anterior forward						
Sebasti -Forcada 2014	31	120.3 (45.66)	30	79.8 (45.66)		40.50 [17.58, 63.42]
2 Abduction						
Sebasti -Forcada 2014	31	112.9 (38.56)	30	78.7 (38.56)		34.20 [14.84, 53.56]



Analysis 9.1. Comparison 9 Deltoid-split versus deltopectoral approaches for plate fixation, Outcome 1 Re-operation.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 9 Deltoid-split versus deltopectoral approaches for plate fixation

Outcome: 1 Re-operation

Study or subgroup	Deltoid-split n/N	Deltopectoral n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 For complication or a fall				
Buecking 2014 (1)	9/60	8/60		1.13 [0.47, 2.72]
2 Plate removal by patient request				
Buecking 2014	9/48	8/42		0.98 [0.42, 2.32]

(1) in one case in each group a re-operation resulted from a fall on the shoulder

Analysis 9.2. Comparison 9 Deltoid-split versus deltopectoral approaches for plate fixation, Outcome 2 Dead at 1 year.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 9 Deltoid-split versus deltopectoral approaches for plate fixation

Outcome: 2 Dead at 1 year

Study or subgroup	Deltoid-split n/N	Deltopectoral n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Buecking 2014	1/60	3/60		0.33 [0.04, 3.11]

Analysis 9.3. Comparison 9 Deltoid-split versus deltopectoral approaches for plate fixation, Outcome 3 Complications.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 9 Deltoid-split versus deltopectoral approaches for plate fixation

Outcome: 3 Complications

Study or subgroup	Deltoid-split n/N	Deltopectoral n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Injurious fall on shoulder				
Buecking 2014 (1)	1/60	1/60		1.00 [0.06, 15.62]
2 Axillary nerve damage				
Buecking 2014 (2)	0/60	0/60		Not estimable
3 Screw perforation				
Buecking 2014 (3)	3/60	0/60		7.00 [0.37, 132.66]
4 Implant (head or shaft) loosening				
Buecking 2014 (4)	5/60	6/60		0.83 [0.27, 2.58]
5 Deep infection				
Buecking 2014 (5)	0/60	1/60		0.33 [0.01, 8.02]
6 Humeral head necrosis				
Buecking 2014 (6)	0/60	0/60		Not estimable

(1) Both were associated with postsurgical delirium and resulted in a re-operation

(2) The 1 case resulted in implant removal

(3) All 3 were treated with joint replacement

(4) Group 1: all treated with joint replacement; Group 2: 2 joint replacement, 4 with osteosythesis

(5) The 1 case resulted in implant removal

(6) The 1 case resulted in implant removal

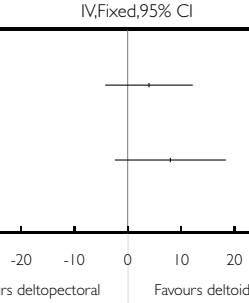
Analysis 9.4. Comparison 9 Deltoid-split versus deltopectoral approaches for plate fixation, Outcome 4 Constant score (0 to 100: best score).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 9 Deltoid-split versus deltopectoral approaches for plate fixation

Outcome: 4 Constant score (0 to 100: best score)

Study or subgroup	Deltoid-split N	Mean(SD)	Deltopectoral N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 At 6 months						
Buecking 2014	48	68 (18.94)	42	64 (20.86)		4.00 [-4.28, 12.28]
2 At 12 months						
Buecking 2014	48	81 (22.39)	42	73 (27.28)		8.00 [-2.40, 18.40]



Analysis 9.5. Comparison 9 Deltoid-split versus deltopectoral approaches for plate fixation, Outcome 5 Pain (VAS 0 to 10: intolerable pain).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 9 Deltoid-split versus deltopectoral approaches for plate fixation

Outcome: 5 Pain (VAS 0 to 10: intolerable pain)

Study or subgroup	Deltoid-split N	Mean(SD)	Deltopectoral N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 At 6 months						
Buecking 2014	48	2.7 (2.24)	42	3.1 (2.4)		-0.40 [-1.36, 0.56]
2 At 12 months						
Buecking 2014	48	1.8 (2.07)	42	2.5 (2.41)		-0.70 [-1.63, 0.23]

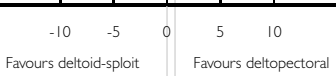
Analysis 9.6. Comparison 9 Deltoid-split versus deltopectoral approaches for plate fixation, Outcome 6 Operation and fluoroscopic times.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 9 Deltoid-split versus deltopectoral approaches for plate fixation

Outcome: 6 Operation and fluoroscopic times

Study or subgroup	Deltoid-split N	Mean(SD)	Deltopectoral N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Duration of operation (minutes)						
Buecking 2014	60	62 (19.76)	60	67 (25.69)		-5.00 [-13.20, 3.20]
2 X-ray exposure (minutes)						
Buecking 2014	60	2 (1.58)	60	1.6 (1.58)		0.40 [-0.17, 0.97]

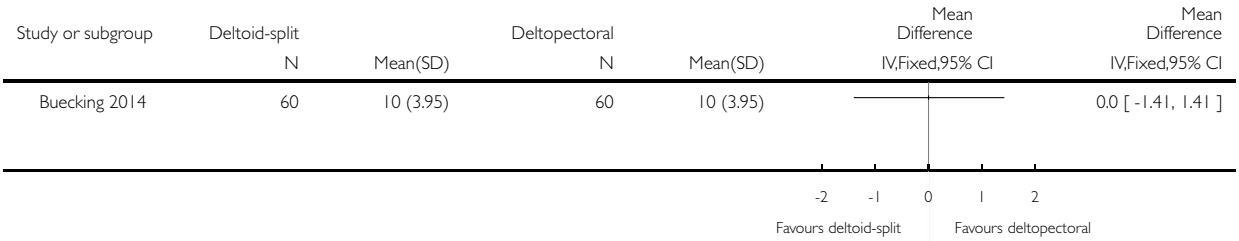


Analysis 9.7. Comparison 9 Deltoid-split versus deltopectoral approaches for plate fixation, Outcome 7 Length of hospital stay (days).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 9 Deltoid-split versus deltopectoral approaches for plate fixation

Outcome: 7 Length of hospital stay (days)

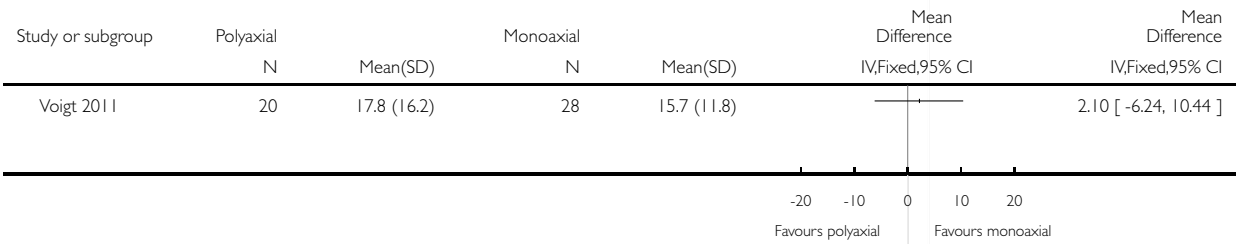


Analysis 10.1. Comparison 10 Polyaxial versus monoaxial screw insertion in plate fixation, Outcome 1 DASH score at 12 months (0 to 100: greatest disability).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 10 Polyaxial versus monoaxial screw insertion in plate fixation

Outcome: 1 DASH score at 12 months (0 to 100: greatest disability)



Analysis 10.2. Comparison 10 Polyaxial versus monoaxial screw insertion in plate fixation, Outcome 2 Simple shoulder test (0 to 12: best outcome).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 10 Polyaxial versus monoaxial screw insertion in plate fixation

Outcome: 2 Simple shoulder test (0 to 12: best outcome)

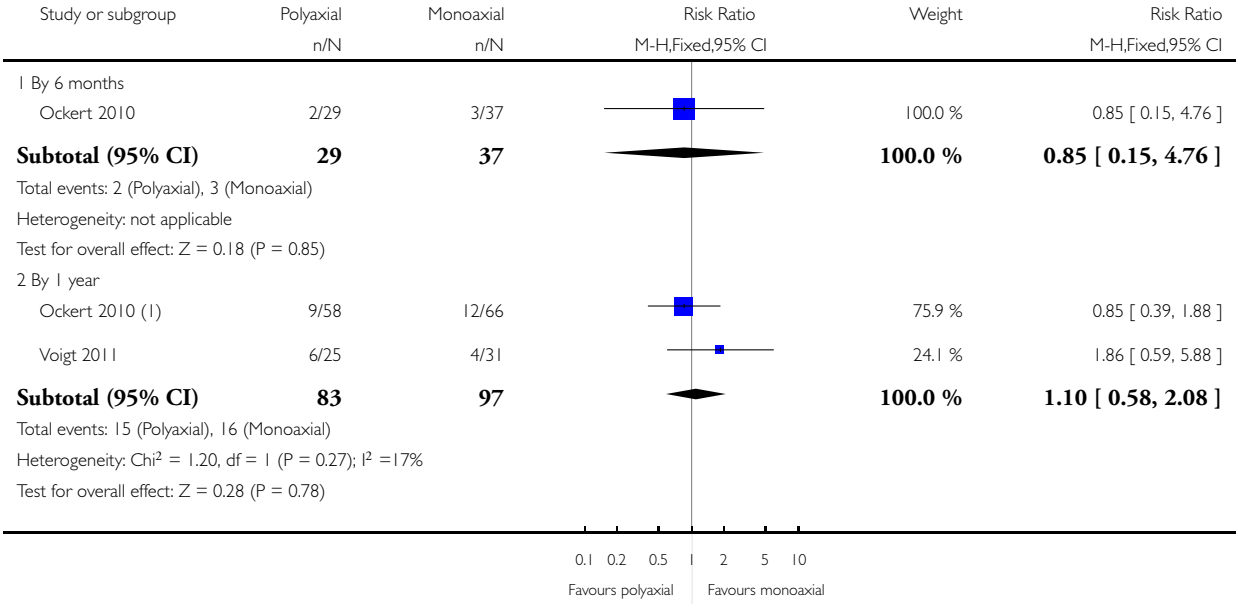
Study or subgroup	Polyaxial N	Mean(SD)	Monoaxial N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 At 3 months						
Voigt 2011	20	5.8 (3)	28	6.9 (2.2)		-1.10 [-2.65, 0.45]
2 At 6 months						
Voigt 2011	20	7.4 (2.9)	28	8 (2.6)		-0.60 [-2.19, 0.99]
3 At 12 months						
Voigt 2011	20	8.6 (3.2)	28	9.7 (1.8)		-1.10 [-2.65, 0.45]

Analysis 10.3. Comparison 10 Polyaxial versus monoaxial screw insertion in plate fixation, Outcome 3 Re-operation.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 10 Polyaxial versus monoaxial screw insertion in plate fixation

Outcome: 3 Re-operation



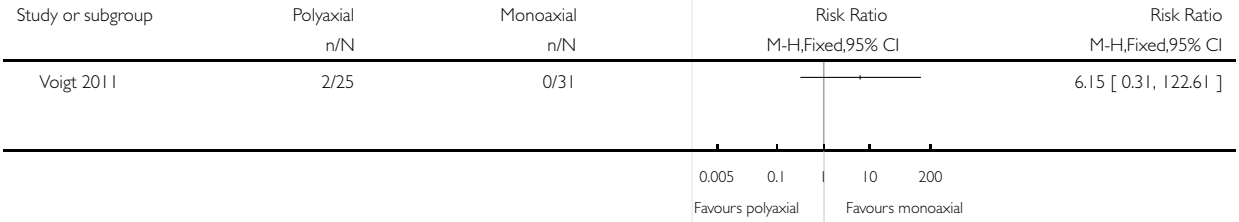
(1) Data from extended trial published 2014

Analysis 10.4. Comparison 10 Polyaxial versus monoaxial screw insertion in plate fixation, Outcome 4 Dead at 1 year.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 10 Polyaxial versus monoaxial screw insertion in plate fixation

Outcome: 4 Dead at 1 year



Analysis 10.5. Comparison 10 Polyaxial versus monoaxial screw insertion in plate fixation, Outcome 5 Constant score at 12 months (% of contralateral limb).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 10 Polyaxial versus monoaxial screw insertion in plate fixation

Outcome: 5 Constant score at 12 months (% of contralateral limb)

Study or subgroup	Polyaxial N	Mean(SD)	Monoaxial N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Voigt 2011	20	73 (17)	28	81 (13)		-8.00 [-16.87, 0.87]

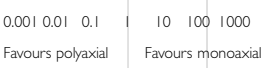
Analysis 10.6. Comparison 10 Polyaxial versus monoaxial screw insertion in plate fixation, Outcome 6 Complications (radiological assessment).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 10 Polyaxial versus monoaxial screw insertion in plate fixation

Outcome: 6 Complications (radiological assessment)

Study or subgroup	Polyaxial n/N	Monoaxial n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Any complication				
Voigt 2011	6/20	8/28		1.05 [0.43, 2.56]
2 Primary implant malposition				
Voigt 2011	0/20	1/28		0.46 [0.02, 10.75]
3 Secondary loss of reduction and screw perforation				
Voigt 2011	6/20	7/28		1.20 [0.47, 3.03]
4 Non-union / delayed union due to osteonecrosis (6 months)				
Ockert 2010	1/29	0/37		3.80 [0.16, 89.98]
5 Avascular necrosis at 1 year				
Voigt 2011	3/20	2/28		2.10 [0.39, 11.43]
6 Varus deformity (> 10 / ≥20 degrees)				
Ockert 2010	8/29	11/37		0.93 [0.43, 2.00]



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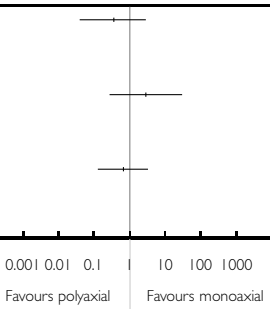
Study or subgroup	Polyaxial n/N	Monoaxial n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Voigt 2011	1/20	4/28		0.35 [0.04, 2.90]
7 Greater tuberosity displacement				
Voigt 2011	2/20	1/28		2.80 [0.27, 28.80]
8 Screw cut-out (intra-articular)				
Ockert 2010	2/29	4/37		0.64 [0.13, 3.24]



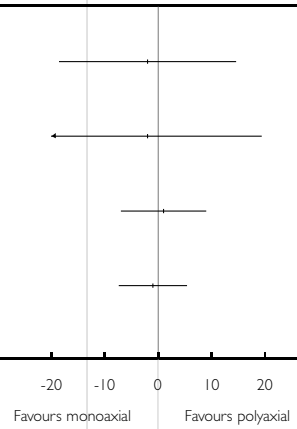
Analysis 10.7. Comparison 10 Polyaxial versus monoaxial screw insertion in plate fixation, Outcome 7 Range of motion (degrees) at 12 months.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 10 Polyaxial versus monoaxial screw insertion in plate fixation

Outcome: 7 Range of motion (degrees) at 12 months

Study or subgroup	Polyaxial N	Mean(SD)	Monoaxial N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Flexion						
Voigt 2011	20	138 (31)	28	140 (26)		-2.00 [-18.65, 14.65]
2 Abduction						
Voigt 2011	20	104 (38)	28	106 (36)		-2.00 [-23.33, 19.33]
3 External rotation						
Voigt 2011	20	41 (12)	28	40 (16)		1.00 [-6.92, 8.92]
4 Internal rotation						
Voigt 2011	20	69 (12)	28	70 (10)		-1.00 [-7.43, 5.43]



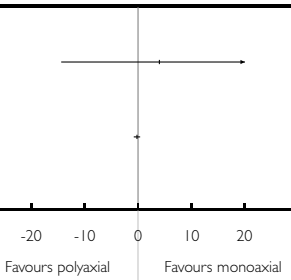
Analysis 10.8. Comparison 10 Polyaxial versus monoaxial screw insertion in plate fixation, Outcome 8 Operation and fluoroscopic times.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 10 Polyaxial versus monoaxial screw insertion in plate fixation

Outcome: 8 Operation and fluoroscopic times

Study or subgroup	Polyaxial N	Mean(SD)	Monoaxial N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Duration of operation (minutes)						
Voigt 2011	20	92 (33)	28	88 (31)		4.00 [-14.47, 22.47]
2 Fluoroscopic time (minutes)						
Voigt 2011	20	1.2 (0.7)	28	1.4 (1.6)		-0.20 [-0.87, 0.47]



Analysis 11.1. Comparison 11 Medial support screws versus control for locking plate fixation, Outcome 1 Adverse events.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 11 Medial support screws versus control for locking plate fixation

Outcome: 1 Adverse events

Study or subgroup	Medial screws n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Early loss of fixation				
Zhang 2011	1/29	9/39		0.15 [0.02, 1.11]
2 Re-operation for early failure				
Zhang 2011	1/29	6/39		0.22 [0.03, 1.76]
3 Osteonecrosis (asymptomatic)				
Zhang 2011	1/29	0/39		4.00 [0.17, 94.79]

Analysis 11.2. Comparison 11 Medial support screws versus control for locking plate fixation, Outcome 2 Constant score (0 to 100: best) at 2.5 years.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 11 Medial support screws versus control for locking plate fixation

Outcome: 2 Constant score (0 to 100: best) at 2.5 years

Study or subgroup	Medial screws N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Zhang 2011	29	79.1 (13.1)	39	70.1 (14.5)		9.00 [2.41, 15.59]

Analysis 12.1. Comparison 12 MultiLoc Proximal Humeral Nail (MPHN) versus Polarus nail, Outcome 1 Adverse events.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 12 MultiLoc Proximal Humeral Nail (MPHN) versus Polarus nail

Outcome: 1 Adverse events

Study or subgroup	MPHN n/N	Polarus n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Re-operation				
Lopiz 2014 (1)	3/26	11/26		0.27 [0.09, 0.87]
2 Post-op impingement				
Lopiz 2014	2/26	5/26		0.40 [0.09, 1.88]
3 Screw loosening				
Lopiz 2014	1/26	7/26		0.14 [0.02, 1.08]
4 Non-union				
Lopiz 2014 (2)	0/26	1/26		0.33 [0.01, 7.82]
5 Rotator cuff symptoms				
Lopiz 2014	9/26	19/26		0.47 [0.27, 0.84]
6 Intra-operative complications				
Lopiz 2014	0/26	0/26		Not estimable
7 Mortality				

(*Continued* . . .)

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Study or subgroup	MPHN n/N	Polarus n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Lopiz 2014	1/28	0/26		2.79 [0.12, 65.66]
8 Radiographic malunion				
Lopiz 2014	3/26	5/26		0.60 [0.16, 2.26]

(1) Straight: 1 screw % 2 nail removals; Curved: 7 screw and 4 nail removals (1 to arthroplasty)

(2) Non-union eventually resulted in a reverse shoulder replacement

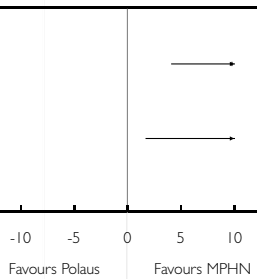
Analysis 12.2. Comparison 12 MultiLoc Proximal Humeral Nail (MPHN) versus Polarus nail, Outcome 2 Constant score (0 to 100: best outcome) at 14 months (6 to 22 months).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 12 MultiLoc Proximal Humeral Nail (MPHN) versus Polarus nail

Outcome: 2 Constant score (0 to 100: best outcome) at 14 months (6 to 22 months)

Study or subgroup	MPHN N	Mean(SD)	Polarus N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Unadjusted Constant score						
Lopiz 2014	26	61.2 (9.3)	26	51.4 (11.5)		9.80 [4.12, 15.48]
2 Adjusted Constant score						
Lopiz 2014	26	83.3 (16.7)	26	72.7 (16)		10.60 [1.71, 19.49]



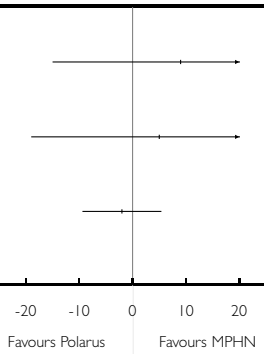
Analysis 12.3. Comparison 12 MultiLoc Proximal Humeral Nail (MPHN) versus Polarus nail, Outcome 3 Range of shoulder motion (degrees).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 12 MultiLoc Proximal Humeral Nail (MPHN) versus Polarus nail

Outcome: 3 Range of shoulder motion (degrees)

Study or subgroup	MPHN N	Mean(SD)	Polarus N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Lateral elevation						
Lopiz 2014	26	124 (53)	26	115 (33)		9.00 [-15.00, 33.00]
2 Forward flexion						
Lopiz 2014	26	132 (46)	26	127 (42)		5.00 [-18.94, 28.94]
3 External rotation						
Lopiz 2014	26	29 (12)	26	31 (15)		-2.00 [-9.38, 5.38]



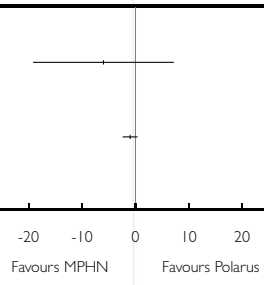
Analysis 12.4. Comparison 12 MultiLoc Proximal Humeral Nail (MPHN) versus Polarus nail, Outcome 4 Lengths of surgery and hospital stay.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 12 MultiLoc Proximal Humeral Nail (MPHN) versus Polarus nail

Outcome: 4 Lengths of surgery and hospital stay

Study or subgroup	MPHN N	Mean(SD)	Polarus N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Length of surgery (minutes)						
Lopiz 2014	26	98 (17)	26	104 (30)		-6.00 [-19.25, 7.25]
2 Length of hospital stay (days)						
Lopiz 2014	26	3 (2)	26	4 (3)		-1.00 [-2.39, 0.39]



Analysis 13.1. Comparison 13 Hemiarthoplasty: EPOCA prosthesis versus HAS prosthesis, Outcome 1 Adverse events.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 13 Hemiarthoplasty: EPOCA prosthesis versus HAS prosthesis

Outcome: 1 Adverse events

Study or subgroup	EPOCA prosthesis n/N	HAS prosthesis n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Deep infection				
Fialka 2008	2/18	0/17		4.74 [0.24, 92.07]
2 Persistent pain - scheduled for reoperation				
Fialka 2008	0/18	2/17		0.19 [0.01, 3.68]

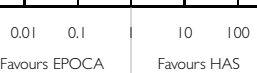
Analysis 13.2. Comparison 13 Hemiarthoplasty: EPOCA prosthesis versus HAS prosthesis, Outcome 2 Radiological assessment findings.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 13 Hemiarthoplasty: EPOCA prosthesis versus HAS prosthesis

Outcome: 2 Radiological assessment findings

Study or subgroup	EPOCA prosthesis n/N	HAS prosthesis n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Resorption of tuberosities				
Fialka 2008	2/18	8/17		0.24 [0.06, 0.96]
2 Secondary dislocation of tuberosities				
Fialka 2008	0/18	0/17		Not estimable
3 Superior migration of prosthesis				
Fialka 2008	2/18	11/17		0.17 [0.04, 0.66]
4 Anterior subluxations				
Fialka 2008	3/18	1/17		2.83 [0.33, 24.66]
5 Glenoid erosion				
Fialka 2008	1/18	6/17		0.16 [0.02, 1.18]
6 Aseptic loosening of stem				
Fialka 2008	0/18	0/17		Not estimable



Analysis 13.3. Comparison 13 Hemiarthoplasty: EPOCA prosthesis versus HAS prosthesis, Outcome 3 Range of motion results at one year (degrees).

Range of motion results at one year (degrees)

Study	**Measure**	**EPOCA prosthesis n = 18**	**HAS prosthesis n = 17**	**Reported significance**
Fialka 2008	Active forward flexion	mean = 109° range = 30° to 150°	mean = 62° range = 20° to 110°	P < 0.001
Fialka 2008	Active abduction	mean = 101° range = 30° to 150°	mean = 62° range = 30° to 100°	P = 0.001
Fialka 2008	Active external rotation in 90° abduction	mean = 30° range = 0° to 60°	mean = 17° range = 0° to 40°	P = 0.01
Fialka 2008	Active external rotation in 90° abduction	mean = 45° range = 0° to 70°	mean = 13° range = 0° to 40°	P = 0.001

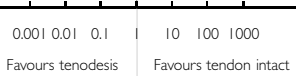
Analysis 14.1. Comparison 14 Hemiarthroplasty: tenodesis of long head of biceps (LHB) versus LHB tendon left intact, Outcome 1 Complications and further surgery.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 14 Hemiarthroplasty: tenodesis of long head of biceps (LHB) versus LHB tendon left intact

Outcome: 1 Complications and further surgery

Study or subgroup	Tenodesis of LHB n/N	LHB tendon intact n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Any complication				
Soliman 2013 (1)	4/23	4/22		0.96 [0.27, 3.36]
2 Further surgery for listed complications				
Soliman 2013 (2)	0/23	1/22		0.32 [0.01, 7.45]
3 Deep infection				
Soliman 2013 (3)	0/23	1/22		0.32 [0.01, 7.45]
4 Tuberosity malunion				
Soliman 2013 (4)	2/23	1/22		1.91 [0.19, 19.63]
5 Inferior subluxation of prosthesis				
Soliman 2013 (5)	1/23	1/22		0.96 [0.06, 14.37]
6 Loss of reduction of greater tuberosity				
Soliman 2013 (6)	1/23	1/22		0.96 [0.06, 14.37]



(1) There is a disparity between the number of participants with complications and total individual complications

(2) This was debridement for deep infection

(3) All cases were mild pain (discomfort) except 2 moderate pain in LBT left intact group

(4) All cases were mild pain (discomfort) except 2 moderate pain in LBT left intact group

(5) All cases were mild pain (discomfort) except 2 moderate pain in LBT left intact group

(6) All cases were mild pain (discomfort) except 2 moderate pain in LBT left intact group

Analysis 14.2. Comparison 14 Hemiarthroplasty: tenodesis of long head of biceps (LHB) versus LHB tendon left intact, Outcome 2 Constant score (0 to 100: best function) at 2 years.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 14 Hemiarthroplasty: tenodesis of long head of biceps (LHB) versus LHB tendon left intact

Outcome: 2 Constant score (0 to 100: best function) at 2 years

Study or subgroup	Tenodesis of LHB		LHB tendon intact		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI	IV,Fixed,95% CI
Soliman 2013	19	74.4 (6.5)	18	69.8 (6.6)		4.60 [0.38, 8.82]

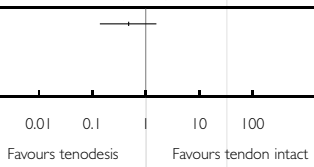
Analysis 14.3. Comparison 14 Hemiarthroplasty: tenodesis of long head of biceps (LHB) versus LHB tendon left intact, Outcome 3 Shoulder pain at 2 year follow-up.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 14 Hemiarthroplasty: tenodesis of long head of biceps (LHB) versus LHB tendon left intact

Outcome: 3 Shoulder pain at 2 year follow-up

Study or subgroup	Tenodesis of LHB	LHB tendon intact	Risk Ratio	Risk Ratio
	n/N	n/N	M-H,Fixed,95% CI	M-H,Fixed,95% CI
Soliman 2013 (1)	3/19	6/18		0.47 [0.14, 1.62]



(1) All cases were mild pain (discomfort) except 2 moderate pain in LBT left intact group

Analysis 14.4. Comparison 14 Hemiarthroplasty: tenodesis of long head of biceps (LHB) versus LHB tendon left intact, Outcome 4 Active shoulder elevation (degrees) at 2 years.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 14 Hemiarthroplasty: tenodesis of long head of biceps (LHB) versus LHB tendon left intact

Outcome: 4 Active shoulder elevation (degrees) at 2 years

Study or subgroup	Tenodesis of LHB		LHB tendon intact		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI	IV,Fixed,95% CI
Soliman 2013	19	152.1 (18.4)	18	149.7 (15.8)		2.40 [-8.63, 13.43]

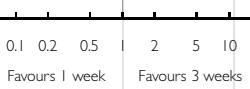
Analysis 15.1. Comparison 15 Post-operative (percutaneous fixation) immobilisation for 1 week versus 3 weeks, Outcome 1 Neer score $\leq$ 80 points (unsatisfactory or failure) at 6 months.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 15 Post-operative (percutaneous fixation) immobilisation for 1 week versus 3 weeks

Outcome: 1 Neer score $\leq$ 80 points (unsatisfactory or failure) at 6 months

Study or subgroup	1 week	3 weeks	Risk Ratio	Risk Ratio
	n/N	n/N	M-H,Fixed,95% CI	M-H,Fixed,95% CI
Wirbel 1999	9/32	10/32		0.90 [0.42, 1.92]



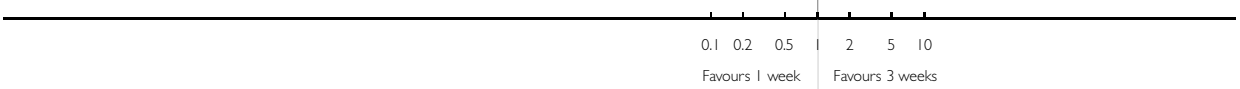
Analysis 15.2. Comparison 15 Post-operative (percutaneous fixation) immobilisation for 1 week versus 3 weeks, Outcome 2 Premature removal of Kirschner wires.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 15 Post-operative (percutaneous fixation) immobilisation for 1 week versus 3 weeks

Outcome: 2 Premature removal of Kirschner wires

Study or subgroup	1 week	3 weeks	Risk Ratio	Risk Ratio
	n/N	n/N	M-H,Fixed,95% CI	M-H,Fixed,95% CI
Wirbel 1999	5/32	5/32		1.00 [0.32, 3.12]



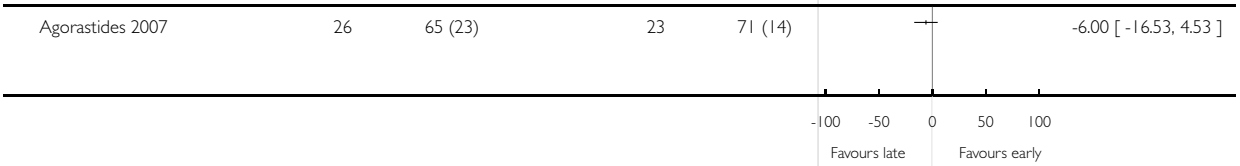
Analysis 16.1. Comparison 16 Post-operative (hemiarthroplasty) mobilisation: early (2 weeks immobilisation) versus late (6 weeks), Outcome 1 Oxford Shoulder Score at 1 year (adjusted: 0 to 100 best).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 16 Post-operative (hemiarthroplasty) mobilisation: early (2 weeks immobilisation) versus late (6 weeks)

Outcome: 1 Oxford Shoulder Score at 1 year (adjusted: 0 to 100 best)

Study or subgroup	Early (after 2 weeks)		Late (after 6 weeks)		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI	IV,Fixed,95% CI
Agorastides 2007	26	65 (23)	23	71 (14)		-6.00 [-16.53, 4.53]



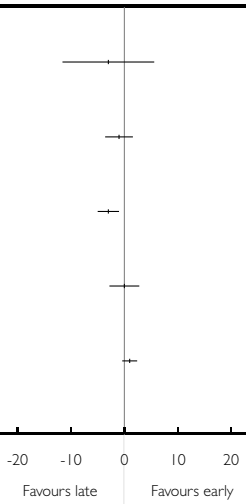
Analysis 16.2. Comparison 16 Post-operative (hemiarthroplasty) mobilisation: early (2 weeks immobilisation) versus late (6 weeks), Outcome 2 Constant shoulder score (at 1 year).

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 16 Post-operative (hemiarthroplasty) mobilisation: early (2 weeks immobilisation) versus late (6 weeks)

Outcome: 2 Constant shoulder score (at 1 year)

Study or subgroup	Early (after 2 weeks) N	Mean(SD)	Late (after 6 weeks) N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Overall score (0 to 100: best)						
Agorastides 2007	26	47 (19)	23	50 (11)		-3.00 [-11.58, 5.58]
2 Pain component (0 to 15: best))						
Agorastides 2007	26	10 (5)	23	11 (4)		-1.00 [-3.52, 1.52]
3 Activities of daily living component (0 to 25: best)						
Agorastides 2007	26	13 (4)	23	16 (3)		-3.00 [-4.97, -1.03]
4 Mobility component (0 to 40: best)						
Agorastides 2007	26	18 (5)	23	18 (5)		0.0 [-2.81, 2.81]
5 Strength component (0 to 25: best)						
Agorastides 2007	26	6 (3)	23	5 (2)		1.00 [-0.41, 2.41]



Analysis 16.3. Comparison 16 Post-operative (hemiarthroplasty) mobilisation: early (2 weeks immobilisation) versus late (6 weeks), Outcome 3 Radiological assessment findings.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 16 Post-operative (hemiarthroplasty) mobilisation: early (2 weeks immobilisation) versus late (6 weeks)

Outcome: 3 Radiological assessment findings

Study or subgroup	Early (after 2 weeks) n/N	Late (after 6 weeks) n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Non-union (with bone resorption)				
Agorastides 2007	2/26	0/23		4.44 [0.22, 88.04]
2 Malunion				
Agorastides 2007	1/26	1/23		0.88 [0.06, 13.35]
3 Greater tuberosity migration (all had severe pain at 6 % 12 months)				
Agorastides 2007	3/26	1/23		2.65 [0.30, 23.77]
4 Superior luxation of prosthesis				
Agorastides 2007	6/26	4/23		1.33 [0.43, 4.12]

Analysis 16.4. Comparison 16 Post-operative (hemiarthroplasty) mobilisation: early (2 weeks immobilisation) versus late (6 weeks), Outcome 4 Range of motion at 1 year.

Review: Interventions for treating proximal humeral fractures in adults

Comparison: 16 Post-operative (hemiarthroplasty) mobilisation: early (2 weeks immobilisation) versus late (6 weeks)

Outcome: 4 Range of motion at 1 year

Study or subgroup	Early (after 2 weeks) N	Mean(SD)	Late (after 6 weeks) N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Elevation (degrees)						
Agorastides 2007	26	80 (17)	23	78 (13)		2.00 [-6.42, 10.42]
2 External rotation (degrees)						
Agorastides 2007	26	14 (7)	23	18 (10)		-4.00 [-8.89, 0.89]

ADDITIONAL TABLES

Table 1. Surgical versus non-surgical treatment trials: brief characteristics

Study	Participants (Neer classification)	Surgery	Non-surgical (starting with)	Follow-up
Boons 2012	50 participants with 4-part fractures (The Netherlands)	Humeral head replacement with the Global prostheses; cemented	Sling immobilisation	1 year
Fjalestad 2010	50 participants with 3- or 4-part fractures (Norway)	Open reduction and fixation with an interlocking plate device and metal cerclages	Immobilisation of the injured arm in a modified Velpeau bandage. Closed reduction in 8 patients	2 years
Kristiansen 1988	30 participants with 31 2-, 3- or 4-part fractures. Included 7 2-part, 19 3-part and 5 4-part fractures (Denmark)	Percutaneous reduction and external fixation	Closed manipulation and sling immobilisation	2 years
Olerud 2011a	60 participants with 3-part fractures (all had displaced surgical neck fracture) (Sweden)	Open reduction and fixation with a PHILOS plate and non-absorbable sutures	Sling immobilisation	2 years
Olerud 2011b	55 participants with 4-part fractures (Sweden)	Humeral head replacement with the Global Fx prosthesis	Sling immobilisation	2 years
ProFHER 2015	250 participants with "displaced fracture of the proximal humerus that involved the surgical neck". Included 18 1-part (but confirmed as still "displaced"), 128 2-part, 93 3-part and 11 4-part fractures (UK)	Either internal fixation (majority were PHILOS plates) or joint replacement (hemiarthroplasty) Pragmatic trial - choice based on surgeon's experience with method	Sling immobilisation	2 years
Stableforth 1984	32 participants with 4-part fracture (UK)	Hemiarthroplasty	Closed manipulation and sling	6 months
Zyto 1997	40 participants with 3- or 4-part fractures (3 others excluded) (Sweden)	Internal fixation using surgical tension band or cerclage wiring	Sling immobilisation	50 months

Table 2. Assessment of items relating to applicability of trial findings

	Clearly defined study population?	Interventions sufficiently described?	Main outcomes sufficiently described?	Appropriate timing of outcome measurement? (Yes = ≥ 1 year)
Agorastides 2007	Partial: exclusions not specified upfront	Yes	Yes	Yes: 1 year
Bertoft 1984	Partial: no exclusion criteria given (e.g. ability to understand instructions for exercises)	Yes	Yes	Yes: 1 year
Boons 2012	Yes	Yes	Yes	Yes: 1 year
Buecking 2014	Partial: indication for hemiarthroplasty poorly defined (27 excluded before randomisation because "implantation of a prosthesis was planned")	Yes	Yes	Yes: 1 year
Cai 2012	Partial: unclear definition of 4-part fractures.	Yes: however, time to surgery not reported	Yes	Yes: 2 years
Fialka 2008	Yes	Yes	Yes	Yes: 1 year
Fjalestad 2010	Yes	Yes	Yes	Yes: 2 years
Hoellen 1997	Yes: but some question over fracture type in that the Holbein 1999 report included 3-part fractures too	Yes	Yes	Yes: 1 year
Hodgson 2003	Yes	Yes	Yes	Yes: 2 years
Kristiansen 1988	Partial: no exclusion criteria given	Partial: incomplete description of timing of sling use and care of external fixator pin sites	Partial: no description of measurement procedures	Yes: 1 year
Kristiansen 1989	Partial: no exclusion criteria given	Partial: although sling and body bandage are common expressions, some variation possible	Partial: no description of measurement procedures	Yes: 2 years
Lefevre-Colau 2007	Yes	Yes	Yes	Partial: 6 months

Table 2. Assessment of items relating to applicability of trial findings (*Continued*)

Livesley 1992	Yes: although this included 4 patients under 20 years with epiphyseal fractures	Yes	Yes	Partial: 6 months
Lopiz 2014	Partial: insufficient criteria given in terms of suitability for surgery	Yes	Yes	Partial: minimum 6 months
Lundberg 1979	Partial: no exclusion criteria given (e.g. ability to understand instructions for exercises)	Yes	Yes	Yes: 1 year or above (mean: 16 months)
Ockert 2010	Partial: exclusion criteria described in context of post-randomisation exclusions	Yes	Yes	Partial: 6 months
Olerud 2011a	Yes	Yes	Yes	Yes: 2 years
Olerud 2011b	Yes	Yes	Yes	Yes: 2 years
ProFHER 2015	Yes	Yes In the context of this being a pragmatic trial	Yes	Yes: 2 years
Revay 1992	Yes	Partial: frequency of swimming sessions not stated	Yes	Yes: 1 year
Rommens 1993	Yes: but to note that other fractures including rib (3 participants) were included	Yes	Partial: functional outcome assessment not described (sufficiently)	No: only until fracture consolidation
Sebastiá-Forcada 2014	Yes	Yes	Yes	Yes: minimum 2 years
Smejkal 2011	Yes	Partial: Only minimal intra-operative details given and nothing regarding post-operative management including rehabilitation	Partial: this may have been 'lost in translation' (Czech article)	Yes: mean 2 years but range not stated (probably most/all > 1 year as recruitment had finished January 2010)
Soliman 2013	No: no explanation given for a younger population; insufficient criteria given in terms of suitability for	Yes	Partial: incomplete description of pain categories; no clarification	Yes: minimum 21 months follow-up

Table 2. Assessment of items relating to applicability of trial findings (*Continued*)

	hemiarthroplasty		of modification to Constant score	
Stableforth 1984	Yes	Yes	Partial: no description of measurement procedures, incomplete description of pain categories	Partial: up to 6 months, then between 18 months to 12 years. This is too spread out. Most results applied to the 6-month follow-up
Torrens 2012	Partial: the < 1.5 cm criterion for posterior displacement of the greater tuberosity is unusual and no justification was given by the authors	Partial: incomplete description of accompanying "progressive rehabilitation program"	Partial: incomplete description of measurement procedures	Yes: 1 year
Voigt 2011	Yes	Yes	Yes	Yes: 1 year
Wirbel 1999	Yes	Yes	Partial: no description of measurement procedures	Partial: between 9 and 36 months; < 1 year in 10 participants. Main results applied to 6 months
Zhang 2011	Yes	Yes	Partial: Insufficient information on measurement of complications and timing of their measurement	Yes: All over 25 months (mean 30.8 months)
Zhu 2011	Yes	Yes	Yes	Yes: 1 and 3 years
Zyto 1997	Yes	Yes	Yes	Yes: 1 year, and 3 to 5 years

APPENDICES

Appendix 1. Search strategies January 2012 to November 2014

The Cochrane Library (Wiley Online Library)

#1 MeSH descriptor: [Shoulder Fractures] explode all trees (63)
#2 MeSH descriptor: [Humeral Fractures] explode all trees (85)
#3 MeSH descriptor: [Humerus] explode all trees (63)
#4 (shoulder* or humor*) (5000)
#5 fract* (27727)
#6 (#3 or #4) (5000)
#7 (#1 or #2) (148)
#8 (#5 and #6) (759)
#9 (#7 or #8) Publication Year from 2011 to 2012 (91) [Trials]

MEDLINE (OVID Online)

1 Shoulder Fractures/ (2387)
2 Humeral Fractures/ (6074)
3 ((humor$ or shoulder$) adj10 (fracture$ or fixat$)).tw. (8248)
4 or/2-3 (10515)
5 (proximal or neck$1 or sub?capital).tw. (316523)
6 and/4-5 (2718)
7 or/1,6 (3865)
8 Randomized controlled trial.pt. (399438)
9 Controlled clinical trial.pt. (90638)
10 randomized.ab. (318613)
11 placebo.ab. (163586)
12 Drug therapy.fs. (1782347)
13 randomly.ab. (228361)
14 trial.ab. (332305)
15 groups.ab. (1435899)
16 or/8-15 (3524227)
17 exp Animals/ not Humans/ (4090273)
18 16 not 17 (3026698)
19 7 and 18 (402)
20 (2012$ or 2013$ or 2014$).ed. (2951048)
21 19 and 20 (114)

EMBASE (OVID Online)

1 Humerus Fracture/ (7941)
2 ((humer$ or shoulder$) adj10 (fract$ or fixat$)).tw. (9383)
3 or/1-2 (12152)
4 (proximal or neck$1 or sub?capital).tw. (366908)
5 and/3-4 (3262)
6 exp Randomized Controlled Trial/ (352803)
7 exp Double Blind Procedure/ (116053)
8 exp Single Blind Procedure/ (18999)
9 exp Crossover Procedure/ (40548)
10 Controlled Study/ (4443980)

11 or/6-10 (4522468)
12 ((clinical or controlled or comparative or placebo or prospective$ or randomi#ed) adj3 (trial or study)).tw. (773369)
13 (random$ adj7 (allocat$ or allot$ or assign$ or basis$ or divid$ or order$)).tw. (191210)
14 ((singl$ or doubl$ or trebl$ or tripl$) adj7 (blind$ or mask$)).tw. (164016)
15 (cross?over$ or (cross adj1 over$)).tw. (70584)
16 ((allocat$ or allot$ or assign$ or divid$) adj3 (condition$ or experiment$ or intervention$ or treatment$ or therap$ or control$ or group$)).tw. (251188)
17 or/12-16 (1156434)
18 or/11,17 (5116362)
19 limit 18 to human (3115123)
20 and/5,19 (688)
21 (2012$ or 2013$ or 2014$).em. (4100346)
22 20 and 21 (199)

CINAHL (EBSCO)

S1 (MH "Shoulder Fractures") (642)
S2 (MH "Humeral Fractures") (1,135)
S3 (MH "Humerus/IN/SU") (410)
S4 TX ((humer* or shoulder*)) AND TX ((fracture* or fixat*)) (3,568)
S5 S2 or S3 or S4 (3,751)
S6 TX proximal or neck or subcapital or sub-capital (58,806)
S7 S5 and S6 (935)
S8 S1 or S7 (1,256)
S9 (MH "Clinical Trials+") (180,311)
S10 (MH "Evaluation Research+") (20,829)
S11 (MH "Comparative Studies") (78,838)
S12 (MH "Crossover Design") (12,280)
S13 PT Clinical Trial (76,753)
S14 (MH "Random Assignment") (38,116)
S15 S9 or S10 or S11 or S12 or S13 or S14 (285,418)
S16 TX ((clinical or controlled or comparative or placebo or prospective or randomi?ed) and (trial or study)) (512,070)
S17 TX (random* and (allocat* or allot* or assign* or basis* or divid* or order*)) (68,589)
S18 TX ((singl* or doubl* or trebl* or tripl*) and (blind* or mask*)) (757,946)
S19 TX (crossover* or 'cross over') or TX cross n1 over (15,336)
S20 TX ((allocat* or allot* or assign* or divid*) and (condition* or experiment* or intervention* or treatment* or therap* or control* or group*)) (86,431)
S21 S16 or S17 or S18 or S19 or S20 (1,172,263)
S22 S15 or S21 (1,241,245)
S23 S8 and S22 (474)
S24 EM 2012 OR EM 2013 OR EM 2014 (993,625)
S25 S23 AND S24 (129)

AMED (OVID Online)

1 exp Shoulder/ (1171)
2 exp Humerus/ (115)
3 Fractures Bone/ (790)
4 (fract$ or break$ or broken or ruptur$).tw. (9763)
5 1 or 2 (1265)
6 3 or 4 (9763)
7 5 and 6 (63)
8 ((humer$ or shoulder$) adj10 (fracture$ or fixat$)).tw. (130)

9 7 or 8 (143)
10 (proximal or neck$1 or sub?capital).tw. (5084)
11 9 and 10 (42)
12 (2012$ or 2013$ or 2014$).up. (30025)
13 11 and 12 (5)

Other searches

PEDro
Simple search
1. proximal AND humer* (17 records)
2. neck AND humer* = (8 records)
Advanced search
3. Abstract and title: fracture*
Body part: upper arm, shoulder or shoulder girdle
Method: Clinical trial (30 records)
The Bone and Joint Journal Orthopaedic Proceedings
Title "proximal humer*" and full text or abstract or title "random*" limited to Orthopaedic Proceedings (13 records)
WHO International Clinical Trials Registry Platform Search Portal
1. proximal and humer* (58 records)
2. neck and humer* (3 records)
ISRCTN registry
1. proximal and humer* (38 records)
2. neck AND humer* (28 records)
ClinicalTrials.gov
(proximal OR neck) AND humerus (50 records)

Appendix 2. Numbers and status of studies in the published versions of the review

Version	Trial status	Changes
Ist version Issue 1, 2001	The original review had 9 included studies, 4 excluded studies and 6 studies listed as ongoing	
2nd version (substantive update) Issue 2, 2002	This update had 10 included studies, 9 excluded studies, 3 studies listed as ongoing and 1 study awaiting assessment	Of the four newly identified studies, one (Stableforth 1984) was included, one (Warnecke 1999) was excluded, one (Dias 2001) listed as ongoing, and the other (Martin 2000) placed in Studies Awaiting Assessment. Further information obtained from trialists resulted in the exclusion of four trials that had been previously listed as ongoing studies. Three (Brownson 2001; Hems 2000; Wallace 2000) of these had been set up as a multicentre study to test the Halder nail (Halder 2001), and one (Welsh 2000) had been set up to compare surgical with conservative treatment

(*Continued*)

3rd version (minor update) Issue 3, 2002	As above	Note: this update included some changes to the Discussion in response to comments received from an external reviewer
4th version (substantive update) Issue 4, 2003	This update had 12 included studies, 11 excluded studies, and 4 studies listed as ongoing	Of four newly identified studies, one (Wirbel 1999) was included, one (de Boer 2003) excluded, and two (Frostick 2003; Shah 2003) are listed as ongoing. The other newly included trial (Hodgson 2003) was formerly listed as an ongoing trial. A trial (Martin 2000), previously in 'Studies awaiting assessment', was excluded. Limited additional findings from newly identified trial reports were included for Hoellen 1997
5th version (minor update) Issue 2, 2007	This update had 12 included studies, 12 excluded studies, 5 studies listed as ongoing and 4 pending assessment	Six new studies were identified, one (Fjalestad 2007) was listed as ongoing, one (Flannery 2006) was excluded and the other four were placed in 'Studies awaiting assessment', pending further information
6th version (new citation update) Issue 12, 2010	This update had 16 included studies, 18 excluded studies, 11 studies listed as ongoing and 4 pending assessment	Sixteen new studies were identified. Of these, one (Fialka 2008) was included, four (Gradl 2009; Mechlenburg 2009; Wan 2005; Yang 2006) were excluded, 10 (Brorson 2009; HURA; Liverpool (renamed as Sinopidis 2010 in the next update); NCT00438633; NCT00818987; NCT00999193; NCT01086202; NCT01113411; ProCon; ProFHER 2015) were placed in ongoing trials and one (Luo 2008) awaits assessment. New reports or information resulted in the inclusion of three more trials (Agorastides 2007: former ongoing study Frostick 2003; Fjalestad 2010: former ongoing study Fjalestad 2007; and Lefevre-Colau 2007: formerly Lefevre-colau 2006, a study awaiting assessment); and the exclusion of two studies (Bing 2002: former ongoing trial Sharma 2000; Dias 2001: former ongoing trial Dias 2001 and study awaiting assessment Der Tavitian 2006).
7th version (new citation update) Issue 12, 2012	This update had 23 included studies, 26 excluded studies, 14 studies listed as ongoing and 3 pending assessment	Overall, 18 new studies were identified. Of these, seven (Ockert 2010; Olerud 2011a; Olerud 2011b; Smejkal 2011; Voigt 2011; Zhang 2011; Zhu 2011) were included,

(*Continued*)

		four (Carbone 2012; Edelson 2008; Liao 2009; Zhang 2010) were excluded, five (ACTRN12610000730000; HOMERUS; NCT01557413; NTR3208; TPHF) were placed in ongoing trials and two (Battistella 2011; Fjalestad (RCT proposal)a) await assessment. Further information was obtained for several studies in the previous version (Handoll 2010); this included the one year follow-up report of functional outcome for Fjalestad 2010, and information resulting in the exclusion of Sinopidis 2010, a former ongoing study. Further consideration of Shah 2003, which was listed as an ongoing study, and Pullen 2007, which was awaiting classification, led to their exclusion: it is very unlikely that any further information will be obtained for these trials, including whether they started. Also excluded was Parnes 2005, another study awaiting classification in Handoll 2010; there is currently insufficient evidence to support this being a randomised trial
8th version (new citation update) Issue x, 2015	This update had 31 included studies, 38 excluded studies, 21 studies listed as ongoing and 7 awaiting classification	Overall, 32 new studies were identified. Of these, eight were included (Boons 2012; Buecking 2014; Cai 2012; Lopiz 2014; ProFHER 2015 (5 references, including 1 trial registration and trial protocol); Sebastiá-Forcada 2014; Soliman 2013 (2 references, including 1 trial registration); Torrens 2012 (1 reference and unpublished data)), 12 were excluded (Cigni 2012; Elidrissi 2013; Erdoğan 2014; Fan 2012; IRCT2013052313435N1; Maniscalco 2014a (2 references); Martetschlager 2012; NCT00384852; NCT01532076; NCT02122315; NTR2186; Zuckerman 2012), eight were placed in ongoing trials (NCT01524965; NCT01847508; NCT01984112; NCT02075476; NTR4019; ROTATE (2 references, including 1 trial registration); SHeRPA; Torrens) and four await classification (Liu 2011 (2 papers); NCT02052206; Wang 2013; Zhu 2014). Further information was obtained for several studies in the previous version (Handoll 2012); this included the two-

(*Continued*)

		year follow-up report (Fjalestad 2014a) of functional outcome for Fjalestad 2010, and an additional article (Ockert 2014) , which reported on 48 additional participants for Ockert 2010. A trial registration document and published protocol (Fjalestad 2014b) were found for a newly designated ongoing trial (DELPHI) , previously Fjalestad (RCT proposal), in studies awaiting classification. Published protocols were also found for two ongoing trials (HOMERUS (Verbeek 2012); TPHF (Launonen 2012)). Additional information from updated trial registration documentation was added in for seven ongoing trials (HURA; NCT00438633; NCT00818987; NCT00999193; NCT01113411; NCT01557413; TPHF) . Additional information was also available for Brorson 2009 which was moved from ongoing to studies awaiting classification

Appendix 3. Previous acknowledgements and contribution of authors

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We thank Alastair Gibson for his major contributions to the first four versions of this review and Rajan Madhok for his major contributions to the first five versions of the review.

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Contribution of authors

Rajan Madhok (RM) and Panos Thomas initiated the review and wrote the protocol. Helen Handoll (HH) searched for trials and provided a set of potential studies for inclusion. Alastair Gibson (JNAG) and HH assessed trial quality, tabulated the data and were the main authors of first published version of the review. JNAG, HH and RM contributed to the final manuscript.

For the first and third (both substantive) updates, Helen Handoll initiated the update by extending the search for trials and relevant materials, contacting trialists and preparing the first drafts. JNAG, HH and RM assessed the newly identified trials and contributed to the final manuscripts. All authors contributed to rewording of the discussion in the second minor update (amendment).

For the fourth (minor) update, Helen Handoll initiated the update by extending the search for trials and relevant materials, contacting trialists and preparing the first drafts. RM performed study selection and contributed to the final manuscript.

For the fifth update (sixth version), Helen Handoll initiated the update by extending the search for trials and relevant materials, contacted trialists, revised text and tables to conform to new methodology and formatting requirements, performed risk of bias assessment for already included trials and prepared the first full draft. Both authors piloted forms, performed study selection, and assessed risk of bias and extracted data for the new included trials. Benjamin Ollivere provided feedback on interim drafts and contributed to the final manuscript.

For the sixth update (seventh version), Helen Handoll initiated the update by extending the search for trials and relevant materials, contacted trialists, performed most of data entry and prepared the first full draft. All three authors screened and selected studies, and assessed risk of bias and extracted data for the newly included trials. Katie Rollins also entered data into RevMan. Both Benjamin Ollivere and Katie Rollins provided feedback on interim drafts and contributed to the final manuscript.

WHAT'S NEW

Last assessed as up-to-date: 10 November 2014.

Date	Event	Description
30 October 2015	New citation required and conclusions have changed	1. Changed conclusions for the surgical versus non-surgical intervention comparison. 2. Conclusions changed to accommodate findings of the new comparisons. 3. Change in authorship.
30 October 2015	New search has been performed	In this update, published in Issue 11, 2015, the following changes were made: 1. The full search was updated to November 2014. 2. Overall, 32 new studies were identified. Of these, eight were included, 12 were excluded, eight were placed in ongoing trials and four await classification. Two further reports were identified for two already included trials. Upon identification of a trial registration document and published protocol, one study previously awaiting classification was moved to ongoing. Published protocols were found for two ongoing trials; and additional information from updated trial registration documentation added in for seven ongoing trials. Additional information for one ongoing trial resulted in its transfer from ongoing to studies awaiting classification. 3. Quality of the evidence was assessed using GRADE; two 'Summary of findings' tables added and the Discussion revised and updated.

(*Continued*)

		4. Changes made to the conclusions.

HISTORY

Protocol first published: Issue 1, 1996

Review first published: Issue 1, 2001

Date	Event	Description
22 October 2012	New citation required and conclusions have changed	1. Conclusions changed to accommodate findings of the new comparisons. 2. Change in authorship.
22 October 2012	New search has been performed	In this update, published in Issue 12, 2012, the following changes were made: 1. The full search was updated to January 2012, with other searches extended to June 2012. 2. Eighteen new studies were identified. Of these, seven were included, four were excluded, five were placed in ongoing studies and two await assessment. A new report was available for one already included trial, and contact with a trialist resulted in the exclusion of one study that had been previously listed as ongoing. In the absence of further information after attempts at contact, consideration of one former ongoing study and two studies formerly in 'Studies awaiting assessment' led to their exclusion. 3. Discussion revised and updated. 4. Changes made to the conclusions.
1 November 2010	New citation required and conclusions have changed	1. Conclusions changed to accommodate findings of the new comparisons. 2. Change in authorship.
1 November 2010	New search has been performed	In this update, published in Issue 12, 2010, the following changes occurred: 1. The full search was updated to March 2010; with other searches extended to August 2010. 2. Sixteen new studies were identified, of which one was included, four were excluded, 10 were placed in ongoing trials and one awaits assessment. New reports or information resulted in the inclusion of three more trials and the exclusion of two studies that had been identified previously.

(*Continued*)

		3. Review methods and formatting were updated. 4. Background and Discussion revised and updated. 5. Changes made to the conclusions.
5 August 2008	Amended	Converted to new review format.
28 September 2007	New search has been performed	The fourth update (Issue 2, 2007) included the following: 1. Trial search extended from May 2003 to September 2006. 2. Identification of six new studies: one of which was placed in 'Ongoing studies', one was excluded and the other four are in 'Studies awaiting assessment', pending further information or publication. 3. Various adjustments were made to text, tables and presentation of the analyses to conform to revised methodology and the Cochrane Style Guide: the 'Synopsis' was amended to a 'Plain language summary'; the 'Abstract' was shortened; the 'Objectives' were reworded; methodological quality scores of individual criteria are no longer summed; all totals were removed from the Analyses (Forest plots) and the number of Analyses were reduced by presenting similar outcome measures (e.g. complications) together from the same trial. There was no change to the conclusions of the review.
12 August 2003	New search has been performed	The third update (Issue 4, 2003) included the following: 1. Trial search extended from November 2001 to May 2003. 2. Inclusion of two new trials, one of which had been listed as ongoing. 3. Inclusion of two new ongoing trials. 4. Exclusion of four trials previously listed as ongoing. 5. One trial, previously in pending, was excluded. 6. Addition of limited findings from newly identified trial reports of an already included trial. 7. The conclusions of the review were slightly modified to include the possibility of immediate physiotherapy, without immobilisation, for some types of undisplaced fractures
8 May 2002	Amended	The second update (Issue 3, 2002) included some changes to the Discussion in response to comments received from an external reviewer
15 February 2002	New search has been performed	The first update (Issue 2, 2002) included the following:

(*Continued*)

		1. Trial search extended from July 2000 to November 2001. 2. Inclusion of one new trial. 3. Inclusion of one new ongoing trial. 4. Exclusion of four trials previously listed as ongoing. 5. One trial excluded and another placed in pending. 6. Addition of material from a newly available epidemiological study and commentary on a newly available systematic review. There was no change to the conclusions of the review.

CONTRIBUTIONS OF AUTHORS

For the seventh update (eighth version), Helen Handoll initiated the update by extending the search for trials and relevant materials, contacted trialists, performed most of data entry and prepared the first full draft. Both authors screened and selected studies, assessed risk of bias and extracted data for the newly included trials, and assessed the quality of the evidence using GRADE. Stig Brorson provided feedback on interim drafts and contributed to the final manuscript.

Helen Handoll is the guarantor of the review.

The summaries of the contributions of authors for previous versions of the review are presented in Appendix 3.

DECLARATIONS OF INTEREST

Helen Handoll is a member of the trial management group of ProFHER 2015; an independent review of this trial was performed by Stig Brorson. No other interests to declare.

Stig Brorson was the lead investigator on Brorson 2009. No other interests to declare.

Both authors performed independent study selection on the trial for which the other author was an investigator.

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Internal sources

- University of Teesside, Middlesbrough, UK.

External sources

- National Institute for Health Research, UK.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Update in 2015

The first primary outcome was split into patient-reported shoulder-related scores and patient-reported quality of life scores (see Types of outcome measures).

A key change in terminology was replacing 'conservative' treatment with 'non-surgical' treatment.

We assessed the quality of the evidence using GRADE and, where sufficient evidence was available, prepared 'Summary of findings' tables.

Update in 2012

Statement added to Types of participants clarifying the inclusion of trials with a small proportion of children.

A new secondary outcome was added to Types of outcome measures (composite scores, whether validated or not, of subjectively- and objectively-rated function and overall outcome). This was to distinguish explicitly between validated measures of patient-reported function and activities of daily living and other commonly used composite scores such as the Constant score.

Examples of the secondary outcome 'Other complications' added.

Update in 2010

Most of the changes to methods in Issue 12, 2010 reflected the uptake of new methodology and reporting as described in the Handbook (Higgins 2008b). These include risk of bias assessment and more explicit reporting of data analysis and collection. Types of outcome measures have been revised to define primary and secondary outcomes. Patient-reported measures of upper-limb function and a separate category for serious adverse events have been added.

Update in 2007

The order of the main categories of outcome measures was altered in Issue 2, 2007 to reflect the greater priority given to functional and clinical outcomes.

INDEX TERMS

Medical Subject Headings (MeSH)

Bandages; Fracture Fixation [methods]; Immobilization [methods]; Physical Therapy Modalities; Randomized Controlled Trials as Topic; Self Care; Shoulder Fractures [surgery; *therapy]; Treatment Outcome

MeSH check words

Adult; Humans